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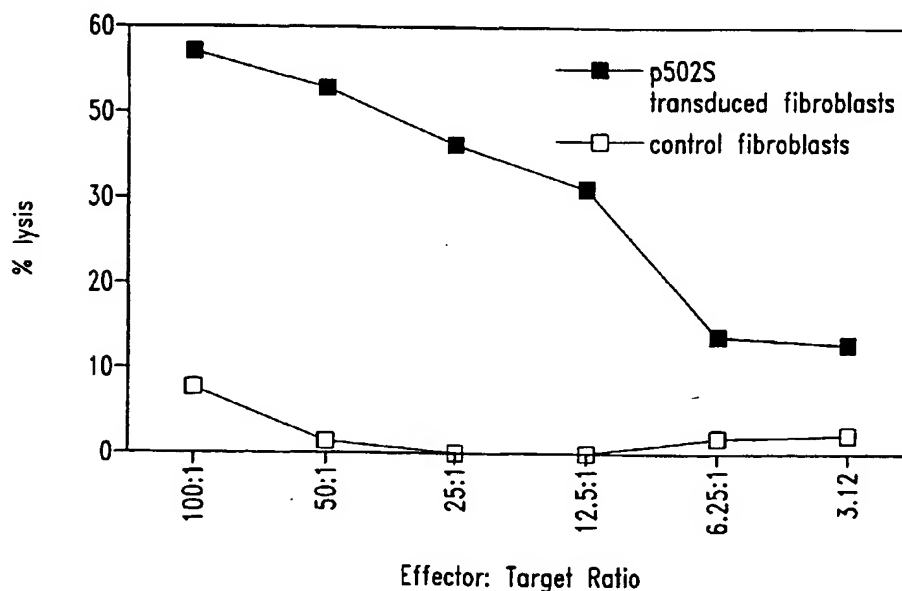
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.



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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of
5 cancer, such as prostate cancer. The invention is more specifically related to
polypeptides, comprising at least a portion of a prostate-specific protein, and to
polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides
are useful in pharmaceutical compositions, *e.g.*, vaccines, and other compositions for
the diagnosis and treatment of prostate cancer.

10 BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although
Cancer is a significant health problem throughout the world. Although advances have
been made in detection and therapy of cancer, no vaccine or other universally successful
method for prevention or treatment is currently available. Current therapies, which are
15 generally based on a combination of chemotherapy or surgery and radiation, continue to
prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with
an estimated incidence of 30% in men over the age of 50. Overwhelming clinical
evidence shows that human prostate cancer has the propensity to metastasize to bone,
20 and the disease appears to progress inevitably from androgen dependent to androgen
refractory status, leading to increased patient mortality. This prevalent disease is
currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate
cancer remains difficult to treat. Commonly, treatment is based on surgery and/or
25 radiation therapy, but these methods are ineffective in a significant percentage of cases.
Two previously identified prostate specific proteins - prostate specific antigen (PSA)
and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic
potential. For example, PSA levels do not always correlate well with the presence of

prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other
5 cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide
10 compositions comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and
15 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-
20 931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;
25

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-

606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of prostate tissue samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for other normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855,

858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858 or 860-862, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant, together with a physiologically acceptable carrier.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

5 Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10 Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

 The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides
15 encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating and/or enhancing the expression,
20 purification and/or immunogenicity of the polypeptide(s).

 Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with prostate cancer, in which case the methods provide
25 treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition as recited above. The patient may be afflicted

with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological
5 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the polypeptide from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological
10 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen presenting cell that
15 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a
20 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a
25 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for
30 determining the presence or absence of a cancer, preferably a prostate cancer, in a

patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide of the present invention, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to an inventive polynucleotide, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample

obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the
5 amount of polynucleotide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more
10 oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

15 BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells
20 expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

25 Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

5 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

 Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

15 Figure 7 is a Western blot showing the expression of P501S in baculovirus.

 Figure 8 illustrates the results of epitope mapping studies on P501S.

 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

 Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

 Figure 11 shows the results of an ELISA assay to determine the specificity of rabbit polyclonal antisera raised against P501S.

 Figures 12A(1), 12A(2), 12A(3), and B are the full-length cDNA (SEQ ID NO:777) and predicted amino acid (SEQ ID NO:778) sequences, respectively, for the clone P788P.

 SEQ ID NO: 1 is the determined cDNA sequence for F1-13

 SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
5 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
10 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
15 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
20 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
25 SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
30 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21

SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
5 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861
SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864
SEQ ID NO: 41 is the determined cDNA sequence for P5
10 SEQ ID NO: 42 is the determined cDNA sequence for P8
SEQ ID NO: 43 is the determined cDNA sequence for P9
SEQ ID NO: 44 is the determined cDNA sequence for P18
SEQ ID NO: 45 is the determined cDNA sequence for P20
SEQ ID NO: 46 is the determined cDNA sequence for P29
15 SEQ ID NO: 47 is the determined cDNA sequence for P30
SEQ ID NO: 48 is the determined cDNA sequence for P34
SEQ ID NO: 49 is the determined cDNA sequence for P36
SEQ ID NO: 50 is the determined cDNA sequence for P38
SEQ ID NO: 51 is the determined cDNA sequence for P39
20 SEQ ID NO: 52 is the determined cDNA sequence for P42
SEQ ID NO: 53 is the determined cDNA sequence for P47
SEQ ID NO: 54 is the determined cDNA sequence for P49
SEQ ID NO: 55 is the determined cDNA sequence for P50
SEQ ID NO: 56 is the determined cDNA sequence for P53
25 SEQ ID NO: 57 is the determined cDNA sequence for P55
SEQ ID NO: 58 is the determined cDNA sequence for P60
SEQ ID NO: 59 is the determined cDNA sequence for P64
SEQ ID NO: 60 is the determined cDNA sequence for P65
SEQ ID NO: 61 is the determined cDNA sequence for P73
30 SEQ ID NO: 62 is the determined cDNA sequence for P75

SEQ ID NO: 63 is the determined cDNA sequence for P76
SEQ ID NO: 64 is the determined cDNA sequence for P79
SEQ ID NO: 65 is the determined cDNA sequence for P84
SEQ ID NO: 66 is the determined cDNA sequence for P68
5 SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred
to as P704P)
SEQ ID NO: 68 is the determined cDNA sequence for P82
SEQ ID NO: 69 is the determined cDNA sequence for U1-3064
SEQ ID NO: 70 is the determined cDNA sequence for U1-3065
10 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692
SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905
SEQ ID NO: 73 is the determined cDNA sequence for V1-3686
SEQ ID NO: 74 is the determined cDNA sequence for R1-2330
SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976
15 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679
SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736
SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738
SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741
SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744
20 SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734
SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774
SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781
SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785
SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787
25 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796
SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807
SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810
SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811
SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876
30 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

- SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896
SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761
SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762
SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766
5 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770
SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771
SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772
SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297
SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309
10 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278
SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288
SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283
SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
15 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12
(also referred to as P504S)
SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
20 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12
(also referred to as P501S)
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-
1862 (also referred to as P503S)
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
25 SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also
referred to as P501S)
SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also
referred to as P503S)
SEQ ID NO: 115 is the determined cDNA sequence for P89
30 SEQ ID NO: 116 is the determined cDNA sequence for P90

SEQ ID NO: 117 is the determined cDNA sequence for P92
SEQ ID NO: 118 is the determined cDNA sequence for P95
SEQ ID NO: 119 is the determined cDNA sequence for P98
SEQ ID NO: 120 is the determined cDNA sequence for P102
5 SEQ ID NO: 121 is the determined cDNA sequence for P110
SEQ ID NO: 122 is the determined cDNA sequence for P111
SEQ ID NO: 123 is the determined cDNA sequence for P114
SEQ ID NO: 124 is the determined cDNA sequence for P115
SEQ ID NO: 125 is the determined cDNA sequence for P116
10 SEQ ID NO: 126 is the determined cDNA sequence for P124
SEQ ID NO: 127 is the determined cDNA sequence for P126
SEQ ID NO: 128 is the determined cDNA sequence for P130
SEQ ID NO: 129 is the determined cDNA sequence for P133
SEQ ID NO: 130 is the determined cDNA sequence for P138
15 SEQ ID NO: 131 is the determined cDNA sequence for P143
SEQ ID NO: 132 is the determined cDNA sequence for P151
SEQ ID NO: 133 is the determined cDNA sequence for P156
SEQ ID NO: 134 is the determined cDNA sequence for P157
SEQ ID NO: 135 is the determined cDNA sequence for P166
20 SEQ ID NO: 136 is the determined cDNA sequence for P176
SEQ ID NO: 137 is the determined cDNA sequence for P178
SEQ ID NO: 138 is the determined cDNA sequence for P179
SEQ ID NO: 139 is the determined cDNA sequence for P185
SEQ ID NO: 140 is the determined cDNA sequence for P192
25 SEQ ID NO: 141 is the determined cDNA sequence for P201
SEQ ID NO: 142 is the determined cDNA sequence for P204
SEQ ID NO: 143 is the determined cDNA sequence for P208
SEQ ID NO: 144 is the determined cDNA sequence for P211
SEQ ID NO: 145 is the determined cDNA sequence for P213
30 SEQ ID NO: 146 is the determined cDNA sequence for P219

SEQ ID NO: 147 is the determined cDNA sequence for P237
SEQ ID NO: 148 is the determined cDNA sequence for P239
SEQ ID NO: 149 is the determined cDNA sequence for P248
SEQ ID NO: 150 is the determined cDNA sequence for P251
5 SEQ ID NO: 151 is the determined cDNA sequence for P255
SEQ ID NO: 152 is the determined cDNA sequence for P256
SEQ ID NO: 153 is the determined cDNA sequence for P259
SEQ ID NO: 154 is the determined cDNA sequence for P260
SEQ ID NO: 155 is the determined cDNA sequence for P263
10 SEQ ID NO: 156 is the determined cDNA sequence for P264
SEQ ID NO: 157 is the determined cDNA sequence for P266
SEQ ID NO: 158 is the determined cDNA sequence for P270
SEQ ID NO: 159 is the determined cDNA sequence for P272
SEQ ID NO: 160 is the determined cDNA sequence for P278
15 SEQ ID NO: 161 is the determined cDNA sequence for P105
SEQ ID NO: 162 is the determined cDNA sequence for P107
SEQ ID NO: 163 is the determined cDNA sequence for P137
SEQ ID NO: 164 is the determined cDNA sequence for P194
SEQ ID NO: 165 is the determined cDNA sequence for P195
20 SEQ ID NO: 166 is the determined cDNA sequence for P196
SEQ ID NO: 167 is the determined cDNA sequence for P220
SEQ ID NO: 168 is the determined cDNA sequence for P234
SEQ ID NO: 169 is the determined cDNA sequence for P235
SEQ ID NO: 170 is the determined cDNA sequence for P243
25 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13
30 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13

SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14

SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-

4736

5 SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-

4738

SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-

4741

SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-

10 4744

SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-

4774

SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-

4781

15 SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-

4785

SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-

4787

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-

20 4796

SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-

4807

SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810

SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811

25 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-

4876

SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-

4884

SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-

30 4896

SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-
4761

SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-
4762

5 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-
4766

SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770
SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-
10 4772

SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-
4309

SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-
4278

15 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-
4288

SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-
4283

SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-
20 4304

SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-
4296

SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-
4280

25 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
30 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
5 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
10 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
SEQ ID NO: 223 is the determined cDNA sequence for P509S
SEQ ID NO: 224 is the determined cDNA sequence for P510S
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
15 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23
20 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
25 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
30 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42

SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
5 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
10 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
15 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3
20 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
25 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
30 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
5 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
10 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
15 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
20 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
25 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
30 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

- SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
5 SEQ ID NO: 307 is the determined cDNA sequence for P711P
SEQ ID NO: 308 is the determined cDNA sequence for P712P
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
SEQ ID NO: 310 is the determined cDNA sequence for P774P
SEQ ID NO: 311 is the determined cDNA sequence for P775P
10 SEQ ID NO: 312 is the determined cDNA sequence for P715P
SEQ ID NO: 313 is the determined cDNA sequence for P710P
SEQ ID NO: 314 is the determined cDNA sequence for P767P
SEQ ID NO: 315 is the determined cDNA sequence for P768P
SEQ ID NO: 316-325 are the determined cDNA sequences of previously
15 isolated genes
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
20 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
SEQ ID NO: 332 is the determined full length cDNA sequence for
P509S
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P
25 (also referred to as 11-C9)
SEQ ID NO: 334 is the determined cDNA sequence for P714P
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also
referred to as 9-F3)
SEQ ID NO: 336 is the predicted amino acid sequence for P705P
30 SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- 5 SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing
homology to Homo sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing
homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- 10 SEQ ID NO: 345 is the determined cDNA sequence for a clone showing
homology to Homo sapiens mRNA for E-cadherin
- SEQ ID NO: 346 is the determined cDNA sequence for a clone showing
homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase
(SHMT)
- 15 SEQ ID NO: 347 is the determined cDNA sequence for a clone showing
homology to Homo sapiens natural resistance-associated macrophage protein2
(NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing
homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)
- 20 SEQ ID NO: 349 is the determined cDNA sequence for a clone showing
homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- SEQ ID NO: 352 is the determined cDNA sequence for P790P
- 25 SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- SEQ ID NO: 357 is the determined cDNA sequence for P745S
- 30 SEQ ID NO: 358 is the determined cDNA sequence for P782P

- SEQ ID NO: 359 is the determined cDNA sequence for P783P
- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- 5 SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- 10 SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the
- 15 sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.
- SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- 20 SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- 25 SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- 30 SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

5 SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor

PDEF.

10 SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

15 SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553 (also known as

P1020C).

20 SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

25 SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

30 SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.
SEQ ID NO:420 is the cDNA sequence for 22581.
SEQ ID NO:421 is the cDNA sequence for 22582.
SEQ ID NO:422 is the cDNA sequence for 22583.
5 SEQ ID NO:423 is the cDNA sequence for 22584.
SEQ ID NO:424 is the cDNA sequence for 22585.
SEQ ID NO:425 is the cDNA sequence for 22586.
SEQ ID NO:426 is the cDNA sequence for 22587.
SEQ ID NO:427 is the cDNA sequence for 22588.
10 SEQ ID NO:428 is the cDNA sequence for 22589.
SEQ ID NO:429 is the cDNA sequence for 22590.
SEQ ID NO:430 is the cDNA sequence for 22591.
SEQ ID NO:431 is the cDNA sequence for 22592.
SEQ ID NO:432 is the cDNA sequence for 22593.
15 SEQ ID NO:433 is the cDNA sequence for 22594.
SEQ ID NO:434 is the cDNA sequence for 22595.
SEQ ID NO:435 is the cDNA sequence for 22596.
SEQ ID NO:436 is the cDNA sequence for 22847.
SEQ ID NO:437 is the cDNA sequence for 22848.
20 SEQ ID NO:438 is the cDNA sequence for 22849.
SEQ ID NO:439 is the cDNA sequence for 22851.
SEQ ID NO:440 is the cDNA sequence for 22852.
SEQ ID NO:441 is the cDNA sequence for 22853.
SEQ ID NO:442 is the cDNA sequence for 22854.
25 SEQ ID NO:443 is the cDNA sequence for 22855.
SEQ ID NO:444 is the cDNA sequence for 22856.
SEQ ID NO:445 is the cDNA sequence for 22857.
SEQ ID NO:446 is the cDNA sequence for 23601.
SEQ ID NO:447 is the cDNA sequence for 23602.
30 SEQ ID NO:448 is the cDNA sequence for 23605.

- SEQ ID NO:449 is the cDNA sequence for 23606.
- SEQ ID NO:450 is the cDNA sequence for 23612.
- SEQ ID NO:451 is the cDNA sequence for 23614.
- SEQ ID NO:452 is the cDNA sequence for 23618.
- 5 SEQ ID NO:453 is the cDNA sequence for 23622.
- SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
- SEQ ID NO:455 is the cDNA sequence for LIM protein.
- SEQ ID NO:456 is the cDNA sequence for a known gene.
- SEQ ID NO:457 is the cDNA sequence for a known gene.
- 10 SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:459 is the cDNA sequence for 23045.
- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for clone 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- 15 SEQ ID NO:468-471 are cDNA sequences for P710P.
- SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 20 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- 25 SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 30

SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

5 SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

10 SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

15 SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

20 SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

25 SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

30 SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.

- SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.
- SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.
- SEQ ID NO: 526 is the full-length cDNA sequence for P790P.
- 5 SEQ ID NO: 527 is the predicted amino acid sequence for P790P.
- SEQ ID NO: 528 & 529 are PCR primers.
- SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.
- SEQ ID NO: 531 is the cDNA sequence of the open reading frame of
- 10 SEQ ID NO: 530.
- SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.
- SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.
- SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ
- 15 ID NO: 533.
- SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.
- SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.
- SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.
- 20 SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.
- SEQ ID NO: 539 is the peptide P501S-370.
- SEQ ID NO: 540 is the peptide P501S-376.
- SEQ ID NO: 541-551 are epitopes of P501S.
- 25 SEQ ID NO: 552 is an extended cDNA sequence for P712P.
- SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.
- SEQ ID NO: 569 is an extended cDNA sequence for P776P.
- SEQ ID NO: 570 is the determined cDNA sequence for a splice variant
- 30 of P776P referred to as contig 6.

SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

5 SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

10 SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

15 SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

20 SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

SEQ ID NO: 594 is a splice variant of P775P referred to as 50717. SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

25 SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

30 SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

5 SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P
and PSA.

SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and
PSA.

10 SEQ ID NO: 618-689 are determined cDNA sequences of prostate-
specific clones.

SEQ ID NO: 690 is the cDNA sequence of the gene DD3.

SEQ ID NO: 691-697 are determined cDNA sequences of prostate-
specific clones.

SEQ ID NO: 698 is an extended cDNA sequence for P714P.

15 SEQ ID NO: 699-701 are the cDNA sequences for splice variants of
P704P.

SEQ ID NO: 702 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-14.

20 SEQ ID NO: 703 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-12.

SEQ ID NO: 704 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-10.

SEQ ID NO: 705 is the cDNA sequence of a spliced variant of P553S
referred to as P553S-6.

25 SEQ ID NO: 706 is the amino acid sequence encoded by SEQ ID NO:
705.

SEQ ID NO: 707 is the amino acid sequence encoded by SEQ ID NO:
702 SEQ ID NO: 708 is a second amino acid sequence encoded by SEQ ID NO: 702.

30 SEQ ID NO: 709-772 are determined cDNA sequences of prostate-
specific clones.

SEQ ID NO: 773 is a first full-length cDNA sequence for prostate-specific transglutaminase gene (also referred to herein as P558S).

SEQ ID NO: 774 is a second full-length cDNA sequence for prostate-specific transglutaminase gene.

5 SEQ ID NO: 775 is the amino acid sequence encoded by the sequence of
SEQ ID NO: 773.

SEQ ID NO: 776 is the amino acid sequence encoded by the sequence of SEQ ID NO: 774.

SEQ ID NO: 777 is the full-length cDNA sequence for P788P.

10 SEQ ID NO: 778 is the amino acid sequence encoded by SEQ ID NO:
777.

SEQ ID NO: 779 is the determined cDNA sequence for a polymorphic variant of P788P.

SEQ ID NO: 780 is the amino acid sequence encoded by SEQ ID NO: 15 779.

SEQ ID NO: 781 is the amino acid sequence of peptide 4 from P703P.

SEQ ID NO: 782 is the cDNA sequence that encodes peptide 4 from P703P.

SEQ ID NO: 783-798 are the cDNA sequence encoding epitopes of
20 P703P.

SEQ ID NO: 799-814 are the amino acid sequences of epitopes of P703P.

SEQ ID NO: 815 and 816 are PCR primers.

SEQ ID NO: 817 is the cDNA sequence encoding an N-terminal portion
25 of P788P expressed in *E. coli*.

SEQ ID NO: 818 is the amino acid sequence of the N-terminal portion of P788P expressed in *E. coli*.

SEQ ID NO: 819 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

30 SEQ ID NO: 820 and 821 are PCR primers.

SEQ ID NO: 822 is the cDNA sequence for the Ra12-P510S-C construct.

SEQ ID NO: 823 is the cDNA sequence for the P510S-C construct.

SEQ ID NO: 824 is the cDNA sequence for the P510S-E3 construct.

5 SEQ ID NO: 825 is the amino acid sequence for the Ra12-P510S-C construct.

SEQ ID NO: 826 is the amino acid sequence for the P510S-C construct.

SEQ ID NO: 827 is the amino acid sequence for the P510S-E3 construct.

SEQ ID NO: 828-833 are PCR primers.

10 SEQ ID NO: 834 is the cDNA sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 835 is the amino acid sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 836 and 837 are PCR primers.

15 SEQ ID NO: 838 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 839 is the determined cDNA sequence for a P703P His tag fusion protein.

SEQ ID NO: 840 and 841 are PCR primers.

20 SEQ ID NO: 842 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 843 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 844 and 845 are PCR primers.

25 SEQ ID NO: 846 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 847 is the determined cDNA sequence for a P711P His tag fusion protein.

30 SEQ ID NO: 848 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 849 and 850 are PCR primers.

SEQ ID NO: 851 is the determined cDNA sequence for the construct Ra12-P501S-E2.

5 SEQ ID NO: 852 is the determined amino acid sequence for the construct Ra12-P501S-E2.

SEQ ID NO: 853 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 854 is the DNA sequence encoding SEQ ID NO: 853.

SEQ ID NO: 855 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 856 is the DNA sequence encoding SEQ ID NO: 855.

10 SEQ ID NO: 857 is a peptide employed in epitope mapping studies.

SEQ ID NO: 858 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 859 is the DNA sequence encoding SEQ ID NO: 858.

SEQ ID NO: 860-862 are the amino acid sequences for CD4 epitopes of P501S.

15 SEQ ID NO: 863-865 are the DNA sequences encoding the sequences of SEQ ID NO: 860-862.

SEQ ID NO: 866-877 are the amino acid sequences for putative CTL epitopes of P703P.

SEQ ID NO: 878 is the full-length cDNA sequence for P789P.

20 SEQ ID NO: 879 is the amino acid sequence encoded by SEQ ID NO: 878.

SEQ ID NO: 880 is the determined full-length cDNA sequence for the splice variant of P776P referred to as contig 6.

25 SEQ ID NO: 881-882 are determined full-length cDNA sequences for the splice variant of P776P referred to as contig 7.

SEQ ID NO: 883-887 are amino acid sequences encoded by SEQ ID NO: 880.

SEQ ID NO: 888-893 are amino acid sequences encoded by the splice variant of P776P referred to as contig 7.

SEQ ID NO: 894 is the full-length cDNA sequence for human transmembrane protease serine 2.

SEQ ID NO: 895 is the amino acid sequence encoded by SEQ ID NO: 894.

5 SEQ ID NO: 896 is the cDNA sequence encoding the first 209 amino acids of human transmembrane protease serine 2.

SEQ ID NO: 897 is the first 209 amino acids of human transmembrane protease serine 2.

10 SEQ ID NO: 898 is the amino acid sequence of peptide 296-322 of P501S.

SEQ ID NO: 899-902 are PCR primers.

SEQ ID NO: 903 is the determined cDNA sequence of the Vb chain of a T cell receptor for the P501S-specific T cell clone 4E5.

15 SEQ ID NO: 904 is the determined cDNA sequence of the Va chain of a T cell receptor for the P501S-specific T cell clone 4E5.

SEQ ID NO: 905 is the amino acid sequence encoded by SEQ ID NO 903.

SEQ ID NO: 906 is the amino acid sequence encoded by SEQ ID NO 904.

20 SEQ ID NO: 907 is the full-length open reading frame for P768P including stop codon.

SEQ ID NO: 908 is the full-length open reading frame for P768P without stop codon.

25 SEQ ID NO: 909 is the amino acid sequence encoded by SEQ ID NO: 908.

SEQ ID NO: 910-915 are the amino acid sequences for predicted domains of P768P.

SEQ ID NO: 916 is the full-length cDNA sequence of P835P.

30 SEQ ID NO: 917 is the cDNA sequence of the previously identified clone FLJ13581.

SEQ ID NO: 918 is the cDNA sequence of the open reading frame for P835P with stop codon.

SEQ ID NO: 919 is the cDNA sequence of the open reading frame for P835P without stop codon.

5 SEQ ID NO: 920 is the full-length amino acid sequence for P835P.

SEQ ID NO: 921-928 are the amino acid sequences of extracellular and intracellular domains of P835P.

SEQ ID NO: 929 is the full-length cDNA sequence for P1000C.

10 SEQ ID NO: 930 is the cDNA sequence of the open reading frame for P1000C, including stop codon.

SEQ ID NO: 931 is the cDNA sequence of the open reading frame for P1000C, without stop codon.

SEQ ID NO: 932 is the full-length amino acid sequence for P1000C.

SEQ ID NO: 933 is amino acids 1-100 of SEQ ID NO: 932.

15 SEQ ID NO: 934 is amino acids 100-492 of SEQ ID NO: 932.

SEQ ID NO: 935-937 are PCR primers.

SEQ ID NO: 938 is the cDNA sequence of the expressed full-length P767P coding region.

20 SEQ ID NO: 939 is the cDNA sequence of an expressed truncated P767P coding region.

SEQ ID NO: 940 is the amino acid sequence encoded by SEQ ID NO: 939.

SEQ ID NO: 941 is the amino acid sequence encoded by SEQ ID NO: 938.

25 SEQ ID NO: 942 is the DNA sequence of a CD4 epitope of P703P.

SEQ ID NO: 943 is the amino acid sequence of a CD4 epitope of P703P.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly prostate cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); Maniatis et al. *Molecular Cloning: A Laboratory Manual* (1982); *DNA Cloning: A Practical Approach*, vol. I & II (D. Glover, ed.); *Oligonucleotide Synthesis* (N. Gait, ed., 1984); *Nucleic Acid Hybridization* (B. Hames & S. Higgins, eds., 1985); *Transcription and Translation* (B. Hames & S. Higgins, eds., 1984); *Animal Cell Culture* (R. Freshney, ed., 1986); Perbal, *A Practical Guide to Molecular Cloning* (1984).

All publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-

expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of
5 this invention are amino acid subsequences comprising epitopes, *i.e.*, antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111,
10 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide
15 sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In specific embodiments, the polypeptides of the invention comprise amino acid sequences as set
20 forth in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

25 The polypeptides of the present invention are sometimes herein referred to as prostate-specific proteins or prostate-specific polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in prostate tissue samples. Thus, a "prostate-specific polypeptide" or "prostate-specific protein," refers generally to a polypeptide sequence of the present
30 invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed

in a substantial proportion of prostate tissue samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of prostate tissue samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in other
5 normal tissues, as determined using a representative assay provided herein. A prostate-specific polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are
10 immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with prostate cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory*
15 *Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

20 As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide.
25 Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they
30 specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other

immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain has been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide composition set forth herein, such as those set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-
5 380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-
10 335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally
15 encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequence set forth herein.

In one preferred embodiment, the polypeptide fragments and variants
20 provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or
25 more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally
30 occurring or may be synthetically generated, for example, by modifying one or more of

the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader
5 sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another
10 amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide
15 with desirable characteristics, *e.g.*, with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino
20 acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence
25 substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its

hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5);
5 glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are
10 within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of
15 its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 \pm 1); glutamate (+3.0 \pm 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5 \pm 1); alanine (−0.5); histidine (−0.5); cysteine
20 (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ± 2
25 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that
30 take various of the foregoing characteristics into consideration are well known to those

of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of
5 flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

10 Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values
15 include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a
20 preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

25 As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For
30 example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be “identical” if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for
10 Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is
15 reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in
20 the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of
25 matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises
30 at least one polypeptide as described herein and an unrelated sequence, such as a known

tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al.,

Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to
5 separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and
10 transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus,
15 tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression
20 and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent
25 and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also*, Skeiky et al., *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the
30 purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous

immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least
5 about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions,
10 additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a
15 portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino
20 acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells.
25 Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is
30 derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine

amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been
5 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at
10 residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention,
15 when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4⁺ T-cells specific for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further
20 described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a
25 growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of
30 the invention are isolated. An "isolated" polypeptide is one that is removed from its

original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99%
5 pure.

Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total
10 genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude
15 genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may
20 be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-
25 to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably an immunogenic variant or derivative, of such a sequence.

5 Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823,
10 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-
15 931, 938, 939 and 942, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In certain preferred
20 embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

 In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-
25 335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this
30 invention using the methods described herein, (*e.g.*, BLAST analysis using standard

parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

5 Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous
10 genes of xenogenic origin.

 In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to, or complementary to, one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at
15 least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103,
20 *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

 In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary
25 sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for
30 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in

the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the
5 exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set
10 forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof,
15 regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by
20 the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

25 When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison
30 window" as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, preferably 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using
5 the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical
10 Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-
15 425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI),
25 or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST
30 2.0 can be used, for example with the parameters described herein, to determine percent

sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present

invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25

nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single
5 stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

10 In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded
15 vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected
20 which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be
25 obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable
5 signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known
10 rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

15 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

20 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 contiguous nucleotides that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence
25 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a
30 sequence of interest will enable them to be of use in detecting the presence of

complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of
5 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in
10 various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger
15 contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in
20 length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

25 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various

factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCRTM technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, *e.g.*, one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to

destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention, polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, striatal GABA_A receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary,

and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure, T_m ,
5 binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary
10 to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997 Sep 1;25(17):3389-402).

The use of an antisense delivery method employing a short peptide
15 vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered
20 into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme
25 molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For
30 example, a large number of ribozymes accelerate phosphoester transfer reactions with a

high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement
5 that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general,
10 enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to
15 cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many
20 technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of
25 target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action
30 (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the

specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis δ virus, group I intron or RNaseP RNA (in association with an RNA
5 guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic
10 Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis δ virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada
et al., Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive,
15 Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have
nucleotide sequences within or surrounding that substrate binding site which impart an
20 RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically
incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as
25 described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that
30 prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO

92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes

expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*,

Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will
5 depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed
10 by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that
15 contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and
20 utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*,
25 Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in
30 diagnostics, modulating protein in organisms, and treatment of conditions susceptible to therapeutics.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

Polynucleotide Identification, Characterization and Expression

Polynucleotide compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena *et al.*, *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller *et al.*, *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

reference in its entirety. Briefly, in PCRTM, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse transcription and PCRTM amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCRTM amplification technique, are readily known and available in the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat. Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification.

- 5 Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

- For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or
10 bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may
15 be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can
20 then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

- Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.*
25 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a
30 known region. The amplified sequences are typically subjected to a second round of

amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

10 In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be

confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

5 In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing
10 sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York.
15 N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid,
20 or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

25 The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription
30 and translation elements, including constitutive and inducible promoters, may be used.

For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of β -galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For

example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of

skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

5 A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal
10 antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; *Serological Methods, a Laboratory Manual*, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

15 A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions
20 thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used
25 include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained
30 intracellularly depending on the sequence and/or the vector used. As will be understood

by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant (K_d) of the interaction, wherein a smaller K_d represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both the "on rate constant" (K_{on}) and the "off rate constant" (K_{off}) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of K_{off}/K_{on} enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant K_d . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable regions" which are interposed between more conserved flanking stretches known as

"framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation

of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab)₂" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V_H::V_L heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad.-Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V_H::V_L heterodimer which is expressed from a gene fusion including V_H- and V_L-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an

antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (*e.g.*, a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRs. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) Nature 349:293-299; Lobuglio et al. (1989) Proc. Nat. Acad. Sci. USA 86:4220-4224; Shaw et al. (1987) J Immunol. 138:4534-4538; and Brown et al. (1987) Cancer Res. 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) Nature 332:323-327; Verhoeyen et al. (1988) Science 239:1534-1536; and Jones et al. (1986) Nature 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) Ann. Rev. Biochem. 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (*e.g.*, electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in

this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred
5 toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a
10 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an
15 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which
20 otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,
25 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of
30 different cleavable linker groups have been described. The mechanisms for the

intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by
5 serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody.
10 Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent
15 bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for
20 radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For
25 example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells

may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et

al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T
5 cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a
10 variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by
15 cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions
20 disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is
25 virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as

described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (*e.g.*, salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (*e.g.*, sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, *e.g.*, vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve

the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (*e.g.*, U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, *e.g.*, U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines* 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129;

Kotin, R. M. (1994) Human Gene Therapy 5:793-801; Shelling and Smith (1994) Gene Therapy 1:165-169; and Zhou et al. (1994) J. Exp. Med. 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, Proc. Natl. Acad. Sci. USA (1990) 87:6743-6747; Fuerst et al. Proc. Natl. Acad. Sci. USA (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer

protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant
5 Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, *e.g.*, WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in
10 U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et
15 al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner
20 et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al.,
25 *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in a specific location and orientation
via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the
30 polynucleotide may be stably maintained in the cell as a separate, episomal segment of

DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression
5 construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable
10 beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK)
15 and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device,
20 propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639
25 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances
30 or potentiates an immune response (antibody and/or cell-mediated) to an exogenous

antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins.

- 5 Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated
10 sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

- Within certain embodiments of the invention, the adjuvant composition
15 is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as
20 provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman,
25 *Ann. Rev. Immunol.* 7:145-173, 1989.

- Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL[®] adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US
30 Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing

oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by
5 Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example
10 combinations of at least two of the following group comprising QS21, QS7, Quil A, β -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix,
15 particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or
20 suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol^R to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

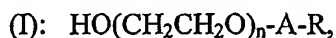
In one preferred embodiment, the adjuvant system includes the
25 combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL[®] adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-

MPL[®] adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn[®]; Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



wherein, n is 1-50, A is a bond or $-\text{C}(\text{O})-$, R is C_{1-50} alkyl or Phenyl C_{1-50} alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein n is between 1 and 50, preferably 4-24, most preferably 9; the R component is C_{1-50} , preferably $\text{C}_4\text{-C}_{20}$ alkyl and most preferably C_{12} alkyl, and A is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12th edition: entry 7717). These adjuvant molecules are described in WO

99/52549. The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

5 According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or
10 maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

15 Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In
20 general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex*
25 *vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

 Dendritic cells and progenitors may be obtained from peripheral blood,
30 bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph

nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated
5 immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration,
10 including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release.
15 In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers
20 include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends
25 upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S.
30 Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763;

5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems. such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, 10 polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

15 The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition 20 may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and 25 formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they

may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 5 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, 10 cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to 15 materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds 20 may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of 25 active compound(s) in each therapeutically useful composition may be prepared in such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a 30 variety of dosages and treatment regimens may be desirable.

For oral administration, the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or

by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride.

- 5 Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered
10 isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml
15 of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity
20 standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for
25 example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be

administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption
5 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase
10 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the
15 lungs *via* nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of
20 a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid
25 particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example,
30 Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998

Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

5 Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery
10 systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

15 In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

 Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the
20 present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for
25 example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of prostate cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous,

intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)

obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the
5 biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in
10 the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c)
15 comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding
20 agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized
25 binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and polypeptide portions thereof to which the binding agent binds, as
30 described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized

on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed

and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

10 To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with
15 samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985,
20 p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a
25 signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10

nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the
5 diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold*
10 *Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules.
15 PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold
20 or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above
25 for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the

cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound
5 binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific
10 for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

15 The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein.
20 Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

25 Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be

present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from
10 prostate tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA
15 was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns
20 (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA
25 libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69% of clones
30 having inserts and the average insert size being 1120 base pairs. For both libraries,

sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor
5 and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol
10 precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the
15 DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of
20 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three
25 more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E.*

coli DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 μ g each of human glandular kallikrein, PSA and

mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

- 5 Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA
- 10 sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively).
- 15 Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike,
- 20 four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant
- 25 homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding

predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A⁺ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807,

1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the
5 isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were
10 over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-
15 4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively,
20 and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA⁺ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297,
25 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-

4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

The determined cDNA sequences for additional prostate-specific clones isolated during characterization of prostate specific cDNA libraries are provided in SEQ ID NO: 618-689, 691-697 and 709-772. Comparison of these sequences with those in the public databases revealed no significant homologies to any of these sequences.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

5 Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

10 Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was
15 used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β-actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β-actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for
20 each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

 mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung
25 tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at
30 high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon

and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at
5 low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

10 Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also
15 expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal
20 muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and
25 kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow,
30 brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney,

ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatazis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. Subsequent comparison of the sequence of SEQ ID NO: 384 with sequences in the public databases, led to the identification of a full-length cDNA sequence of P1000C (SEQ ID NO: 929), which encodes a 492 amino acid sequence.

Analysis of the amino acid sequence using the PSORT II program led to the identification of a putative transmembrane domain from amino acids 84-100. The cDNA sequence of the open reading frame of P1000C, including the stop codon, is provided in SEQ ID NO: 930, with the open reading frame without the stop codon being
5 provided in SEQ ID NO: 931. The full-length amino acid sequence of P1000C is provided in SEQ ID NO: 932. SEQ ID NO: 933 and 934 represent amino acids 1-100 and 100-492 of P1000C, respectively.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by
10 immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

15 The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver,
20 brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that
25 this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC
POLYPEPTIDES BY PCR-BASED SUBTRACTION

5 A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The
10 resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

 Fifty-nine positive clones were sequenced. Comparison of the DNA
15 sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID
20 NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

 Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences
25 which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 699-701.

 Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA
30 sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145,

147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones
5 containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is
10 provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine
15 and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed
20 comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor
25 compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal
30 prostate and prostate tumor, compared to six of twelve other normal tissues tested.

Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and
5 normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-
10 h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in
15 the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

20 mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor
25 and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those
5 in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

10 PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in
15 SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of
20 the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

Using computer algorithms, the following regions of P703P were predicted to represent potential HLA A2-binding CTL epitopes: amino acids 164-172
25 of SEQ ID NO: 525 (SEQ ID NO: 866); amino acids 160-168 of SEQ ID NO: 525 (SEQ ID NO: 867); amino acids 239-247 of SEQ ID NO: 525 (SEQ ID NO: 868); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 869); amino acids 112-120 of SEQ ID NO: 525 (SEQ ID NO: 870); amino acids 155-164 of SEQ ID NO: 525 (SEQ ID NO: 871); amino acids 117-126 of SEQ ID NO: 525 (SEQ ID NO: 872); amino acids
30 164-173 of SEQ ID NO: 525 (SEQ ID NO: 873); amino acids 154-163 of SEQ ID NO:

525 (SEQ ID NO: 874); amino acids 163-172 of SEQ ID NO: 525 (SEQ ID NO: 875); amino acids 58-66 of SEQ ID NO: 525 (SEQ ID NO: 876); and amino acids 59-67 of SEQ ID NO: 525 (SEQ ID NO: 877).

P703P was found to show some homology to previously identified proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor inhibit thrombin receptor activation and thrombin-induced platelet activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. The potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell membrane to promote tumorigenesis or activate a protease-activated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the P703P-receptor interaction may therefore be usefully employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of P703P expression increased with increasing Gleason score, indicating that P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are

provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P

were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 698. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

5 Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

10 Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an
15 ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on
20 chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential
25 open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The
30 full-length sequences for the two forms are provided in SEQ ID NO: 773 and 774, with

the corresponding amino acid sequences being provided in SEQ ID NO: 775 and 776, respectively. The cDNA sequence of SEQ ID NO: 774 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 776). This insert is not present in the sequence of SEQ ID NO: 773.

5 Further studies on P768P (SEQ ID NO: 315) led to the identification of the putative full-length open reading frame (ORF). The cDNA sequence of the ORF with stop codon is provided in SEQ ID NO: 907. The cDNA sequence of the ORF without stop codon is provided in SEQ ID NO: 908, with the corresponding amino acid sequence being provided in SEQ ID NO: 909. This sequence was found to show 86%
10 identity to a rat calcium transporter protein, indicating that P768P may represent a human calcium transporter protein. The locations of transmembrane domains within P768P were predicted using the PSORT II computer algorithm. Six transmembrane domains were predicted at amino acid positions 118-134, 172-188, 211-227, 230-246, 282-298 and 348-364. The amino acid sequences of SEQ ID NO: 910-915 represent
15 amino acids 1-134, 135-188, 189-227, 228-246, 247-298 and 299-511 of P768P, respectively.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

20

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of
25 conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid
30 (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of

0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

5

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF
PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

10 A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide
15 restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

20 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate
25 hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences
30 which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich
5 differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

10 In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for
15 proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA
20 sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant
25 homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most
30 prostate tumors and BPH tissues by a factor of three or greater, with elevated expression

seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

5 Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349,
10 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant
15 homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is
20 shown in Figure 12A (SEQ ID NO: 777), with the corresponding predicted amino acid being shown in Figure 12B (SEQ ID NO: 778). Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 779, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this
25 polymorphic variant of P788P is provided in SEQ ID NO: 779, with the corresponding amino acid sequence being provided in SEQ ID NO: 780. The sequence of SEQ ID NO: 780 differs from that of SEQ ID NO: 778 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively. Further studies led to the isolation of the full-length sequence for the clone of SEQ ID NO: 570 (provided in SEQ ID NO: 880). Full-length cloning efforts on the clone of SEQ ID NO: 571 led to the isolation of two sequences (provided in SEQ ID NO: 881 and 882), representing a single clone, that are identical with the exception of a polymorphic insertion/deletion at position 1293. Specifically, the clone of SEQ ID NO: 882 (referred to as clone F1) has a C at position 1293. The clone of SEQ ID NO: 881 (referred to as clone F2) has a single base pair deletion at position 1293. The predicted amino acid sequences encoded by 5 open reading frames located within SEQ ID NO: 880 are provided in SEQ ID NO: 883-887, with the predicted amino acid sequences encoded by the clone of SEQ ID NO: 881 and 882 being provided in SEQ ID NO: 888-893.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common,

suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

5 The clone of SEQ ID NO: 342 (referred to as P789P) was found to show homology to a previously identified gene. The full length cDNA sequence for P789P and the corresponding amino acid sequence are provided in SEQ ID NO: 878 and 879, respectively.

10

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

15 Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were
20 immunized with 100µg of P2S#12 and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium
25 pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells (5×10^5 /ml) were
30 restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells

(Sherman et al, *Science* 258:815-818, 1992) and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 μ g/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes,

CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

5 Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 μ g of P1S #10 and 120 μ g of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single
10 cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6×10^6 cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2 μ g/ml P1S#10 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 μ g/ml dextran sulfate and 25 μ g/ml LPS for 3 days). Six days later cells (5×10^5 /ml) were restimulated
15 with 2.5×10^6 /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as
20 shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were
25 isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION

WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred
5 to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research
Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012
either intramuscularly or intradermally. The mice were immunized three times, with a
two week interval between immunizations. Two weeks after the last immunization,
immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator
10 cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL
activity was assessed against P501S transduced targets. Two out of 8 mice developed
strong anti-P501S CTL responses. These results demonstrate that P501S contains at
least one naturally processed HLA-A2-restricted CTL epitope.

15 EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate
tumor polypeptide to recognize human tumor.

20 Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ
ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells
according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75,
1998). The resulting CD8⁺ T cell microcultures were tested for their ability to
recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which
25 were transduced to express the P502S gene in a γ -interferon ELISPOT assay (*see*
Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells
were assayed in duplicate on 10⁴ fibroblasts in the presence of 3 µg/ml human β_2 -
microglobulin and 1 µg/ml P2S-12 peptide or control E75 peptide. In addition, T cells
were simultaneously assayed on autologous fibroblasts transduced with the P502S gene
30 or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the

fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES

IN HUMAN BLOOD

20

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts

retrovirally transduced to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (^{51}Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997*). The results of these assays are presented in Figures 6A and 6B.

10

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPIOTOPE CONTAINED WITHIN THE PROSTATE-SPECIFIC ANTIGEN P703P

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 μg of p5 peptide together with 140 μg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the

control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte
5 cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures,
10 CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being
15 recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 781, with the corresponding cDNA sequence being provided in SEQ ID NO: 782.

Twenty 15-mer peptides overlapping by 10 amino acids and derived
20 from the carboxy-terminal fragment of P703P were generated using standard procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration
25 of 0.25 microgram/ml. Pulsed DC were washed and plated at 1×10^4 cells/well of 96-well V-bottom plates and purified CD4 T cells were added at 1×10^5 /well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2.
30 Following 4 *in vitro* stimulation cycles, 96 lines (each line corresponding to one well) were tested for specific proliferation and cytokine production in response to the

stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by ³H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 781). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVSVVS (SEQ ID NO: 781) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVSVVS (SEQ ID NO: 781) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of

recombinant P703P sources were utilized; *E. coli*-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were *E. coli*-derived L3E (a lung-specific antigen) and baculovirus-derived mamaglobin. In interferon-gamma ELISA assays, line 1-F9 was able to efficiently recognize both *E. coli* forms of
5 P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the *E. coli* and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) from P703P is a naturally processed peptide epitope derived from
10 P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above.
15 DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of
20 P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are
25 provided in SEQ ID NO: 799-814, with the corresponding cDNA sequences being provided in SEQ ID NO: 783-798, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity
30 for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cell lines were restimulated on the

appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in *E. coli* (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in *E. coli*. Of the T cell lines tested, line I-1A
5 recognized specifically the truncated form of P703P (*E. coli*) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (*E. coli*) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or
10 were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDLMLIKLDE (SEQ ID NO: 814; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A, and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 811; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 810; corresponding to a.a. 135-149 of
15 SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

In further studies, forty 15-mer peptides overlapping by 10 amino acids and derived spanning amino acids 47 to 254 of P703P (SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was
20 determined essentially as described above. DC were prepared from PBMC of a donor having distinct HLA DR and DQ alleles from that used in previous experiments. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 0.25 microgram/ml, and each pool containing 10 peptides. Twelve lines were identified that demonstrated specific proliferation and cytokine production
25 (measured in gamma-interferon ELISA assays) in response to the stimulating peptide pool. These lines were further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and specific recognition of recombinant P703P protein. Lines 3A5H and 3A9H specifically proliferated and produced gamma-interferon in response to recombinant protein and one individual
30 peptide as well as the peptide pool. Following re-stimulation on targets loaded with the specific peptide, only 3A9H responded specifically to targets exposed to lysates of

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fibroblasts infected adenovirus expressing full-length P703P. These results indicates that the line 3A9H can respond to antigenic peptide derived from protein synthesized in mammalian cells. The peptide to which the specific CD4 line responded correspond to amino acids 155-170 of P703P (SEQ ID NO: 943). The DNA sequence for this peptide is provided in SEQ ID NO: 942.

EXAMPLE 11

EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN

IN PROSTATE

10

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing

Gleason grade, demonstrating that expression of B305D increases as prostate cancer progresses.

EXAMPLE 12

5 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996),
10 human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte
15 cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+
20 T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous
25 fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce
5 Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113,
10 which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing
15 Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive
20 epitope.

In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with
25 recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8⁺ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above
30 background were cloned on autologous EBV-transformed B cells (BLCL), also

transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percoll gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501S-expressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a γ -IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and
5 CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL, pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid sequence of P501S were loaded onto autologous B-LCL and tested in γ -IFN Elispot assays for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5
10 and 4E7. One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer peptides that comprised the positive pool were tested individually in γ -IFN Elispot assays for the ability to stimulate the two P501S-specific CTL clones, 4E5 and
15 4E7. Both 4E5 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 853; cDNA sequence provided in SEQ ID NO: 854) that spanned amino acids 453-472 of P501S. Since the minimal epitope recognized by CD8+ T cells is almost always either a 9 or 10-mer peptide sequence, 10-mer peptides that spanned the entire sequence of SEQ ID NO: 853 were synthesized that differed by 1 amino acid. Each of these 10-mer
20 peptides was tested for the ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer peptide (SEQ ID NO: 855; cDNA sequence provided in SEQ ID NO: 856) was identified that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-472 of P501S. This sequence defines a minimal 10-mer epitope from P501S that can be naturally processed and to which CTL responses
25 can be identified in normal PBMC. Thus, this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of SEQ ID NO: 855, HLA blocking and mismatch analyses were performed. In γ -IFN Elispot assays, the specific response of clones 4A7 and 4E5 to P501S-transduced
30 autologous fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking antibody) and B1.23.2 (HLA-B/C blocking antibody). These results

demonstrate that the SEQ ID NO: 855-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, autologous B-LCL (HLA-A1,A2,B8,B51, Cw1, Cw7) and heterologous B-LCL (HLA-A2,A3,B18,B51,Cw5,Cw14) that share the HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 855, washed, and tested in γ -IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5. Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 855-specific response was detected using both the autologous (D326) and heterologous (D107) B-LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 855 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 855, two 9-mers with the sequences of SEQ ID NO: 857 and 858 were synthesized and tested in Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 855, as well as the 9-mer peptide of SEQ ID NO: 858, but not the 9-mer peptide of SEQ ID NO: 857, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 858 is a 9-mer P501S-derived epitope recognized by P501S-specific CTL. The DNA sequence encoding the epitope of SEQ ID NO: 858 is provided in SEQ ID NO: 859.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 855 and 858 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and co-transfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of

stimulating the P501S-specific CTL to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the
5 subtype of the relevant restricting allele is HLA-B51011.

To determine if the P501S-specific CTL could recognize prostate tumor cells that express P501S, the P501S-positive lines LnCAP and CRL2422 (both expressing "moderate" amounts of P501S mRNA and protein), and PC-3 (expressing low amounts of P501S mRNA and protein), plus the P501S-negative cell line DU-145
10 were retrovirally transduced with the HLA-B51011 allele that was cloned from the donor used to generate the P501S-specific CTL. HLA-B51011- or EGFP-transduced and selected tumor cells were treated with gamma-interferon and androgen (to upregulate stimulatory functions and P501S, respectively) and used in gamma-interferon Elispot assays with the P501S-specific CTL clones 4E5 and 4E7. Untreated
15 cells were used as a control.

Both 4E5 and 4E7 efficiently and specifically recognized LnCAP and CRL2422 cells that were transduced with the HLA-B51011 allele, but not the same cell lines transduced with EGFP. Additionally, both CTL clones specifically recognized PC-3 cells transduced with HLA-B51011, but not the P501S-negative tumor cell line
20 DU-145. Treatment with gamma-interferon or androgen did not enhance the ability of CTL to recognize tumor cells. These results demonstrate that P501S-specific CTL, generated by *in vitro* whole gene priming, specifically and efficiently recognize prostate tumor cell lines that express P501S.

A naturally processed CD4 epitope of P501S was identified as follows.

25 CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1- 325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 µg/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed
30 with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4

stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using γ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4 μ g/ml or an irrelevant peptide at μ g/ml were used as APC. T cell lines that demonstrated either
5 specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

From pool A, lines AD9 and AE10 specifically recognized peptide 1 (SEQ ID NO: 862), and line AF5 recognized peptide 39 (SEQ ID NO: 861). From pool
10 B, line BC6 could be identified that recognized peptide 58 (SEQ ID NO: 860). Each of these lines were stimulated on the specific peptide and tested for specific recognition of the peptide in a titration assay as well as cell lysates generated by infection of HEK 293 cells with adenovirus expressing either P501S or an irrelevant antigen. For these assays, APC-adherent monocytes were pulsed with either 10, 1, or 0.1 μ g/ml individual P501S
15 peptides, and DC were pulsed overnight with a 1:5 dilution of adenovirally infected cell lysates. Lines AD9, AE10 and AF5 retained significant recognition of the relevant P501S-derived peptides even at 0.1 mg/ml. Furthermore, line AD9 demonstrated significant (8.1 fold stimulation index) specific activity for lysates from adenovirus-P501S infected cells. These results demonstrate that high affinity CD4 T cell lines can
20 be generated toward P501S-derived epitopes, and that at least a subset of these T cells specific for the P501S derived sequence of SEQ ID NO: 862 are specific for an epitope that is naturally processed by human cells. The DNA sequences encoding the amino acid sequences of SEQ ID NO: 860-862 are provided in SEQ ID NO: 863-865, respectively.

25 To further characterize the P501S-specific activity of AD9, the line was cloned using anti-CD3. Three clones, referred to as 1A1, 1A9 and 1F5, were identified that were specific for the P501S-1 peptide (SEQ ID NO: 862). To determine the HLA restriction allele for the P501S-specific response, each of these clones was tested in class II antibody blocking and HLA mismatch assays using proliferation and gamma-
30 interferon assays. In antibody blocking assays and measuring gamma-interferon production using ELISA assays, the ability of all three clones to recognize peptide

pulsed APC was specifically blocked by co-incubation with either a pan-class II blocking antibody or a HLA-DR blocking antibody, but not with a HLA-DQ or an irrelevant antibody. Proliferation assays performed simultaneously with the same cells confirmed these results. These data indicate that the P501S-specific response of the clones is restricted by an HLA-DR allele. Further studies demonstrated that the restricting allele for the P501S-specific response is HLA-DRB1501.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

Table ISummary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other

normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 702-705. An amino acid sequence encoded by SEQ ID NO: 705 is provided in SEQ ID NO: 706. The cDNA sequence of SEQ ID NO: 702 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 707 and 708.

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table IIProstate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

- 5 Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the
- 10 Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters
- 15 (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

5 The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels
10 of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes
15 generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

 Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The
20 sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that
5 encodes the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

EXAMPLE 15

10 FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above
15 was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-460 represent novel genes. The others (SEQ ID NO: 454-
20 458 and 461-467) correspond to known sequences. Comparison of the determined

cDNA sequence of SEQ ID NO: 461 with sequences in the Genbank database using the BLAST program revealed homology to the previously identified transmembrane protease serine 2 (TMPRSS2). The full-length cDNA sequence for this clone is provided in SEQ ID NO: 894, with the corresponding amino acid sequence being
5 provided in SEQ ID NO: 895. The cDNA sequence encoding the first 209 amino acids of TMPRSS2 is provided in SEQ ID NO: 896, with the first 209 amino acids being provided in SEQ ID NO: 897.

The sequence of SEQ ID NO: 462 (referred to as P835P) was found to correspond to the previously identified clone FLJ13518 (Accession AK023643; SEQ ID
10 NO: 917), which had no associated open reading frame (ORF). This clone was used to search the Geneseq DNA database and matched a clone previously identified as a G protein-coupled receptor protein (DNA Geneseq Accession A09351; amino acid Geneseq Accession Y92365), that is characterized by the presence of seven transmembrane domains. The sequences of fragments between these domains are
15 provided in SEQ ID NO: 921-928, with SEQ ID NO: 921, 923, 925 and 927 representing extracellular domains and SEQ ID NO: 922, 924, 926 and 928 representing intracellular domains. SEQ ID NO: 921-928 represent amino acids 1-28, 53-61, 83-103, 124-143, 165-201, 226-238, 263-272 and 297-381, respectively, of P835P. The full-length cDNA sequence for P835P is provided in SEQ ID NO: 916. The cDNA
20 sequence of the open reading frame for P835P, including stop codon, is provided in SEQ ID NO: 918, with the open reading frame without stop codon being provided in SEQ ID NO: 919 and the corresponding amino acid sequence being provided in SEQ ID NO: 920.

25

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P
30 fragment described above. One million colonies were plated on LB/Ampicillin plates.

Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 690.

EXAMPLE 17

PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostate-specific antigens in *E. coli*, baculovirus and mammalian cells.

a) Expression of P501S in *E. coli*

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was

cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The
5 resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression
10 was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen
15 Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as
20 Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to
25 aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of
30 the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S

DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The
5 sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C
10 fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 848) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 849) and AW053 (SEQ ID NO: 850). AW042 is a sense
15 cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein
20 was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM β -Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 851 and 852, respectfully.

25 b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the

manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553 amino acids; SEQ ID NO: 113) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The

Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type
5 Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 μ l of GenePorter was diluted in 500 μ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 μ g of plasmid DNA that was diluted in 500 μ l of serum-free media, mixed briefly and incubated for 30 min at room
10 temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera
15 raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

d) Expression of P703P in Baculovirus

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with
20 several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make
25 recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein:

e) Expression of P788P in *E. Coli*

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in *E. coli* as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 815 and 816). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the designed construct. The expression construct P788P-N #6/pCRX1 was transformed into *E. coli* BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD600 of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 817, with the corresponding amino acid sequence being provided in SEQ ID NO: 818.

f) Expression of P510S in *E. coli*

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in *E. coli* as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal end, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 820 and 821, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and

vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A mini-induction screen was performed to optimize the expression conditions. After induction
5 the cells grew well, achieving OD 600 nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin +
10 chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 822 and 825,
15 respectively.

The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to that used for Ra12-P510S-C, except that the PCR primers
20 employed were those shown in SEQ ID NO: 828 and 829, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 828 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 829 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3)
25 CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein sequencing. The optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (+
30 kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow

to grow at 37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-C construct are shown in SEQ ID NO: 823 and 826, respectively.

5 The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in *E. coli* as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 830 and 831. The primer of SEQ ID NO: 830 is a sense primer with an NdeI site for use in ligating into pPDM. The primer of SEQ ID NO: 831 is an antisense primer with an added XhoI site
10 for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing
15 confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3
20 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P501S-E3 construct are provided in SEQ ID NO: 824 and 827, respectively.

g) Expression of P775S in *E. Coli*

The antigen P775P contains multiple open reading frames (ORF). The
25 third ORF, encoding the protein of SEQ ID NO: 483, has the best motif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 832 and the anti-sense PCR primer of SEQ ID NO: 833. The PCR amplified fragment of P775P and

Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after
5 induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 834 and 835, respectively.

10

H) Expression of a P703P His tag fusion protein in *E. coli*

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 836 and 837. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag
15 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 838 and 839, respectively.

20

I) Expression of a P705P His tag fusion protein in *E. coli*

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 840 and 841. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag
25 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 842 and 843, respectively.

30

J) Expression of a P711P His tag fusion protein in *E. coli*

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 844 and 845. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 846 and 847, respectively.

10

K) Expression of P767P in *E. coli*

The full-length coding region of P767P (amino acids 2-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-468 and PDM-469 (SEQ ID NO: 935 and 936, respectively). DNA amplification was performed using 10 µl 10X Pfu buffer, 1 µl 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 66°C for 15 sec and by 72°C for 2 min., and lastly by 1 cycle of 72°C for 4 min. The PCR product was digested with XhoI and cloned into a modified pET28 vector with a histidine tag in frame on the 5' end that was digested with Eco72I and XhoI. The construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The cDNA coding region for the recombinant B767P protein is provided in SEQ ID NO: 938, with the corresponding amino acid sequence being provided in SEQ ID NO: 941. The full-length P767P did not express at high enough levels for detection or purification.

A truncated coding region of P767P (referred to as B767P-B; amino acids 47-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-573 and PDM-469 (SEQ ID NO: 937 and 936, respectively) and the PCR conditions described above for full-length P767P. The PCR product was digested with XhoI and cloned into the modified pET28 vector that was digested with Eco72I and XhoI. The

construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The protein was found to be expressed in the inclusion body pellet. The coding region for the expressed B767P-B protein is provided in SEQ ID NO: 939, with the corresponding amino acid sequence
5 being provided in SEQ ID NO: 940.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

10

a) Preparation and Characterization of Polyclonal Antibodies against P703P, P504S and P509S

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

15 Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml to 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were
20 induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run
25 through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed

inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then vialled after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyl dipeptide (MDP). Every four weeks rabbits were boosted with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250 microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 min. Plates were again

washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H₂SO₄ and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

b) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ($\mu\text{g/ml}$)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

- 5 The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 $\mu\text{g/ml}$, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using
- 10 an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-
- 15 LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described

above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-

mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors,

5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

c) Preparation and Characterization of Antibodies against P503S

5 A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at
 10 Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur

fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

d) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM

technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

5

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

10 Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-
15 514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk^{-/-} cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated
20 from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight
25 since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure

specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

- Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

e) Preparation and Characterization of Antibodies against P504S

- Full-length P504S (SEQ ID NO: 108) was expressed and purified from bacteria essentially as described above for P501S and employed to raise rabbit monoclonal antibodies using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). The anti-P504S monoclonal antibody 13H4 was shown by Western blot to bind to both expressed recombinant P504S and to native P504S in tumor cells.

- Immunohistochemical studies using 13H4 to assess P504S expression in various prostate tissues were performed as described above. A total of 104 cases, including 65 cases of radical prostatectomies with prostate cancer (PC), 26 cases of prostate biopsies and 13 cases of benign prostate hyperplasia (BPH), were stained with the anti-P504S monoclonal antibody 13H4. P504S showed strongly cytoplasmic granular staining in 64/65 (98.5%) of PCs in prostatectomies and 26/26 (100%) of PCs in prostatic biopsies. P504S was stained strongly and diffusely in carcinomas (4+ in 91.2% of cases of PC; 3+ in 5.5%; 2+ in 2.2% and 1+ in 1.1%) and high grade prostatic intraepithelial neoplasia (4+ in all cases). The expression of P504S did not vary with Gleason score. Only 17/91 (18.7%) of cases of NP/BPH around PC and 2/13 (15.4%) of BPH cases were focally (1+, no 2+ to 4+ in all cases) and weakly positive for P504S in large glands. Expression of P504S was not found in small atrophic glands, postatrophic hyperplasia, basal cell hyperplasia and transitional cell metaplasia in either biopsies or prostatectomies. P504S was thus found to be over-expressed in all Gleason scores of prostate cancer (98.5 to 100% of sensitivity) and exhibited only focal positivities in

large normal glands in 19/104 of cases (82.3% of specificity). These findings indicate that P504S may be usefully employed for the diagnosis of prostate cancer.

EXAMPLE 19

5 CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine
10 the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow
15 the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains.
20 Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

25 Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the
30 substitution of the histidine with an asparagine, was synthesized as described above. A

Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisol:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether.

5 The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described
10 above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell
15 sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and
20 stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (*i.e.*, intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

25 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun
30 at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C.

Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant
5 purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral
10 membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the
15 peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated,
20 blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG
25 (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of

SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

In further studies, mouse monoclonal antibodies were raised against amino acids 296 to 322 to P501S, which are predicted to be in an extracellular domain. A/J mice were immunized with P501S/adenovirus, followed by subsequent boosts with an *E. coli* recombinant protein, referred to as P501N, that contains amino acids 296 to 322 of P501S, and with peptide 296-322 (SEQ ID NO: 898) coupled with KLH. The mice were subsequently used for splenic B cell fusions to generate anti-peptide hybridomas. The resulting 3 clones, referred to as 4F4 (IgG1,kappa), 4G5 (IgG2a,kappa) and 9B9 (IgG1,kappa), were grown for antibody production. The 4G5 mAb was purified by passing the supernatant over a Protein A-sepharose column,

followed by antibody elution using 0.2M glycine, pH 2.3. Purified antibody was neutralized by the addition of 1M Tris, pH 8, and buffer exchanged into PBS.

For ELISA analysis, 96 well plates were coated with P501S peptide 296-322 (referred to as P501-long), an irrelevant P775 peptide, P501S-N, P501TR2, P501S-long-KLH, P501S peptide 306-319 (referred to as P501-short)-KLH, or the irrelevant peptide 2073-KLH, all at a concentration of 2 ug/ml and allowed to incubate for 60 minutes at 37 °C. After coating, plates were washed 5X with PBS + 0.1% Tween and then blocked with PBS, 0.5% BSA, 0.4% Tween20 for 2 hours at room temperature. Following the addition of supernatants or purified mAb, the plates were incubated for 60 minutes at room temperature. Plates were washed as above and donkey anti-mouse IgHRP-linked secondary antibody was added and incubated for 30 minutes at room temperature, followed by a final washing as above. TMB peroxidase substrate was added and incubated 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1N H₂SO₄ and the OD was read at 450 nM. All three hybrid clones secreted mAb that recognized peptide 296-322 and the recombinant protein P501N.

For FACS analysis, HEK293 cells were transiently transfected with a P501S/VR1012 expression constructs using Fugene 6 reagent. After 2 days of culture, cells were harvested and washed, then incubated with purified 4G5 mAb for 30 minutes on ice. After several washes in PBS, 0.5% BSA, 0.01% azide, goat anti-mouse Ig-FITC was added to the cells and incubated for 30 minutes on ice. Cells were washed and resuspended in wash buffer including 1% propidium iodide and subjected to FACS analysis. The FACS analysis confirmed that amino acids 296-322 of P501S are in an extracellular domain and are cell surface expressed.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server

(<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al.* 5 *Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

EXAMPLE 20

REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture 15 system as follows.

Cells from the prostate tumor cell line LNCaP were plated at 1.5×10^6 cells/T75 flask (for RNA isolation) or 3×10^5 cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was 20 continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3- 25 G4-D3 and permeabilized cells.

For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM Na_2HPO_4 , 70 mM H_3PO_4 , 30 1 mM EDTA, 1% SDS, 1% BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was

labeled with ^{32}P using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 0.001 M Na_2EDTA), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found to increase in response to androgen treatment.

10

EXAMPLE 21

PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids). The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP

cDNA was cloned into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ ID NO: 617.

- 5 The fusion FOPP was expressed as a single recombinant protein in *E. coli* as follows. The expression plasmid pCRX1FOPP was transformed into the *E. coli* strain BL21-CodonPlus RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml
- 10 chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the
- 15 cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl
- 20 pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing
- 25 FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at - 70 °C.

EXAMPLE 22

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN
PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

5 Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the TaqmanTM procedure using both gene specific primers and probes to determine the levels of gene expression.

10 Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0

15 and subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the TaqmanTM procedure but extending to 50 cycles using

20 forward and reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and β -actin signal. The remaining 2 samples had no detectable β -actin or P501S. No P501S signal was observed in the four normal blood samples tested.

25

EXAMPLE 23

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN
SCID MOUSE-PASSAGED PROSTATE TUMORS

 When considering the effectiveness of antigens in the treatment of

30 prostate cancer, the continued presence of the antigens in tumors during androgen

ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

Two prostate tumors that had metastasized to the bone were removed
5 from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and normal heart as negative controls. In both cases, the specific mRNA was
10 present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

EXAMPLE 24

15 ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH *IN VIVO*

The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

Ten SCID mice were injected subcutaneously with HEK293 cells that expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0
20 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

25

EXAMPLE 25

CHARACTERIZATION OF A T CELL RECEPTOR CLONE FROM A P501S-SPECIFIC T CELL CLONE

30 T cells have a limited lifespan. However, cloning of T cell receptor (TCR) chains and subsequent transfer essentially enables infinite propagation of the T

cell specificity. Cloning of tumor-antigen TCR chains allows the transfer of the specificity into T cells isolated from patients that share the TCR MHC-restricting allele. Such T cells could then be expanded and used in adoptive transfer settings to introduce the tumor antigen specificity into patients carrying tumors that express the antigen. T cell receptor alpha and beta chains from a CD8 T cell clone specific for the prostate-specific antigen P501S were isolated and sequenced as follows.

Total mRNA from 2×10^6 cells from CTL clone 4E5 (described above in Example 12) was isolated using Trizol reagent and cDNA was synthesized. To determine Va and Vb sequences in this clone, a panel of Va and Vb subtype-specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vb sequence that corresponded to the Vb7 subfamily. Furthermore, using cDNA generated from the clone, the Va sequence expressed was determined to be Va6. To clone the full TCR alpha and beta chains from clone 4E5, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows: TCR Valpha-6 5'(sense): GGATCC---GCCGCCACC---ATGTCACCTTTCTAGCCTGCT (SEQ ID NO: 899) BamHI site Kozak TCR alpha sequence TCR alpha 3' (antisense): GTCGAC---TCAGCTGGACCACAGCCGCAG (SEQ ID NO: 900) SalI site TCR alpha constant sequence TCR Vbeta-7. 5'(sense): GGATCC---GCCGCCACC---ATGGGCTGCAGGCTGCTCT (SEQ ID NO: 901) BamHI site Kozak TCR alpha sequence TCR beta 3' (antisense): GTCGAC---TCAGAAATCCTTTCTCTTGAC (SEQ ID NO: 902) SalI site TCR beta constant sequence. Standard 35 cycle RT-PCR reactions were established using cDNA synthesized from the CTL clone and the above primers, employing the proofreading thermostable polymerase PWO (Roche, Nutley, NJ).

The resultant specific bands (approx. 850 bp for alpha and approx. 950 for beta) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing full-length alpha and beta chains were identified, and large scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were submitted

for sequencing. The sequencing reactions demonstrated the cloning of full-length TCR alpha and beta chains with the determined cDNA sequences for the Vb and Va chains being shown in SEQ ID NO: 903 and 904, respectively. The corresponding amino acid sequences are shown in SEQ ID NO: 905 and 906, respectively. The Va sequence was
 5 shown by nucleotide sequence alignment to be 99% identical (347/348) to Va6.2, and the Vb to be 99% identical to Vb7 (336/338).

EXAMPLE 26

CAPTURE OF PROSTATE SPECIFIC CELLS USING

10 THE PROSTATE ANTIGEN P503S

As described above, P503S is found on the surface of prostate cells. Secondary coated microsphere beads specific for mouse IgG were coupled with the purified P503S-specific monoclonal antibody 1D12. The bound P503S antibody was then used to capture HEK cells expressing recombinant P503S. This provides a model
 15 system for prostate-specific cell capture which may be usefully employed in the detection of prostate cells in blood, and therefore in the detection of prostate cancer.

P503S-transfected HEK cells were harvested and redissolved in wash buffer (PBS, 0.1% BSA, 0.6% sodium citrate) at an appropriate volume to give at least
 5⁴ cells per sample. Round bottom Eppendorf tubes were used for all procedures
 20 involving beads. The stock concentrations were as shown below in Table VIII.

Table VIII

Stock concentrations	Sample concentration	Amount needed
Epithelial enrich beads 4 ⁸ beads/ml (DynaL Biotech Inc. Lake Success, NY)	1 ⁷ beads/ml	125 ul stock per 5 ml volume
1D12 ascites antibody 2 mg/ml	0.1 ug/ml (0.1X) to 5 ug/ml (5X) titrations	0.05 ul to 2.5 ul stock per sample
α - Mamma Mu 0.9 mg/ml	1 ug/ml (1X)	1.1 ul stock per sample
Pan-mouse IgG beads 4 ⁸ beads/ml (DynaL Biotech)	1 ⁷ beads/ml	125 ul stock per 5 ml volume

Blocked immunomagnetic beads were pre-washed as follows: all beads needed were pooled and washed once with 1 ml wash buffer. The beads were resuspended in a 3X volume of 1% BSA (v/v) in wash buffer and incubated for 15 min rotating at 4 °C. The beads were then washed three times with 2X volume of wash
5 buffer and resuspended to original volume. Non-blocked beads were pooled, washed three times with 2X volume of wash buffer and resuspended to original volume.

Primary antibody was incubated with secondary beads in a fresh Eppendorf for 30 minutes, rotating at 4 °C. Approximately 200 ul wash buffer was added to increase the total volume for even mixing of the sample. The antibody-bead
10 solution was transferred to a fresh Eppendorf, washed twice with an equal volume of wash buffer and resuspended to original volume. Target cells were added to each sample and incubated for 45 minutes, rotating at 4 °C. The tubes were transferred to a magnet, the supernatant removed, taking care not to agitate the beads, and the samples were washed twice with 1 ml wash buffer. The samples were then ready for RT-PCR
15 using a Dynabeads mRNA direct microkit (DynaL Biotech).

Epithelial cell enrichment was placed in a magnet and supernatant was removed. The epithelial enrichment beads were then resuspended in 100 ul lysis/binding buffer fortified with Rnasin (2 U/ul per sample), and stored at -70 °C until use. Oligo (dT₂₅) Dynabeads were pre-washed as follows: all beads needed were pooled (23
20 ul/sample), washed three times with an excess volume of lysis/binding buffer, and resuspended to original volume. The lysis supernatant was separated with a magnet and transferred to a fresh Eppendorf. 20 ul oligo(dT₂₅) Dynabeads were added per sample and rolled for 5 min at room temperature. Supernatant was separated using a magnet and discarded, leaving the mRNA annealed to the beads. The bead/mRNA
25 complex was washed with buffer and resuspended in cold Tris-HCl.

For RT-PCR, the Tris-HCl supernatant was separated and discarded using MPS. For each sample containing 1⁵ cells or less, the following was added to give a total volume of 30 ul: 14.25 ul H₂O; 1.5 ul BSA; 6 ul first strand buffer; 0.75 mL 10 mM dNTP mix; 3 ul Rnasin; 3 ul 0.1M dTT; and 1.5 ul Superscript II. The resulting
30 solution was incubated for 1 hour at 42 °C, diluted 1:5 in H₂O, heated at 80°C for 2 min

to detach cDNA from the beads, and immediately placed on MPS. The supernatant containing cDNA was transferred to a new tube and stored at -20°C .

Table IX shows the percentage of capture of P503S-transfected HEK cells as determined by RT-PCR.

5

Table IX

	% capture P503S-transfected HEK cells	% capture LnCAP cells
0.1 ug/ml P503S Mab	36.90	0.00
0.5 ug/ml P503S Mab	67.40	2.93
1 ug/ml P503S Mab	40.22	0.00
5 ug/ml P503S Mab	13.11	0.00
Anti-Mu beads only, non-blocked	1.42	0.00
Anti-Mu beads only, blocked	15.65	20.21
Absolute control, non-capture cells	100.00	100.00

10

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(b) sequences having at least 70% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(c) sequences having at least 90% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(d) sequences encoded by a polynucleotide of claim 1;

(e) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(f) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;
- (c) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591,

593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 2,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

13. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

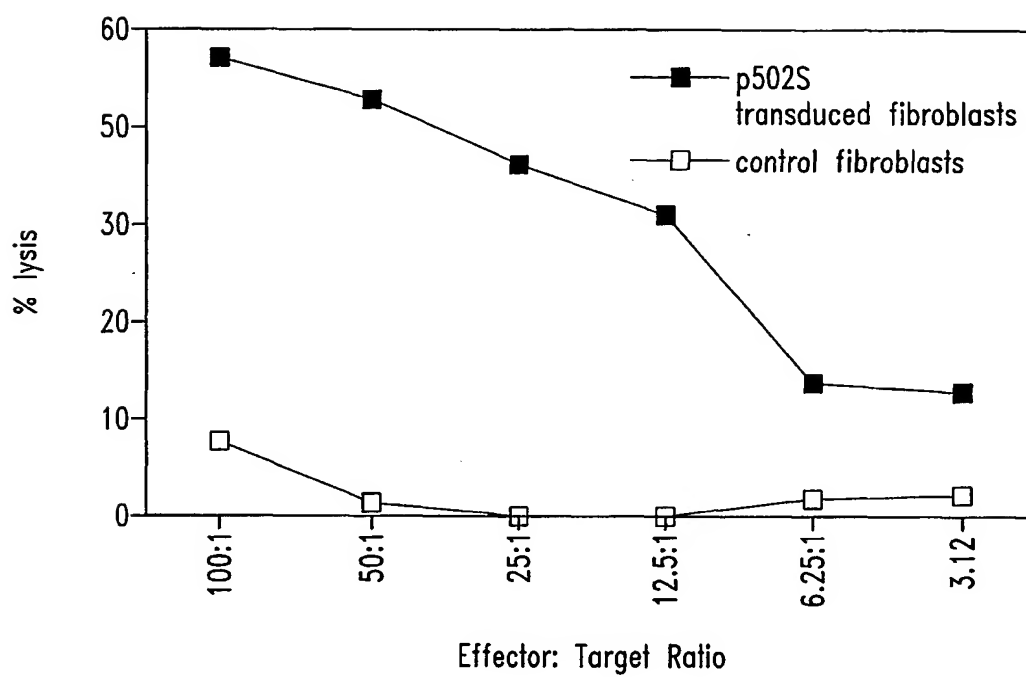
15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

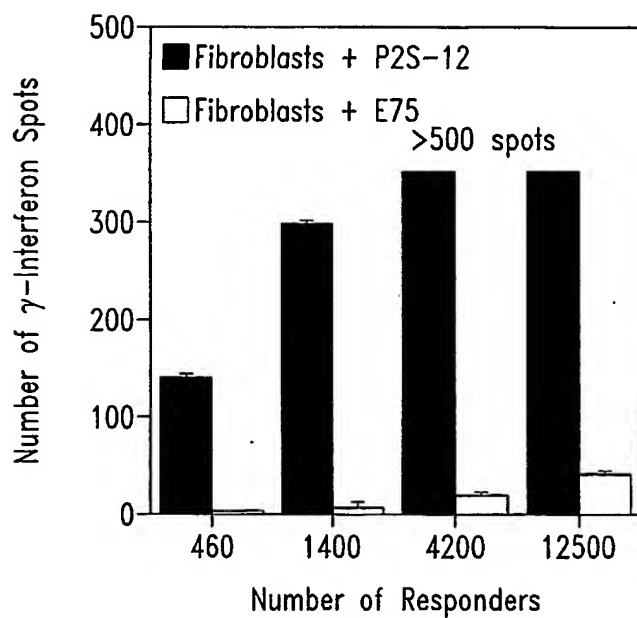
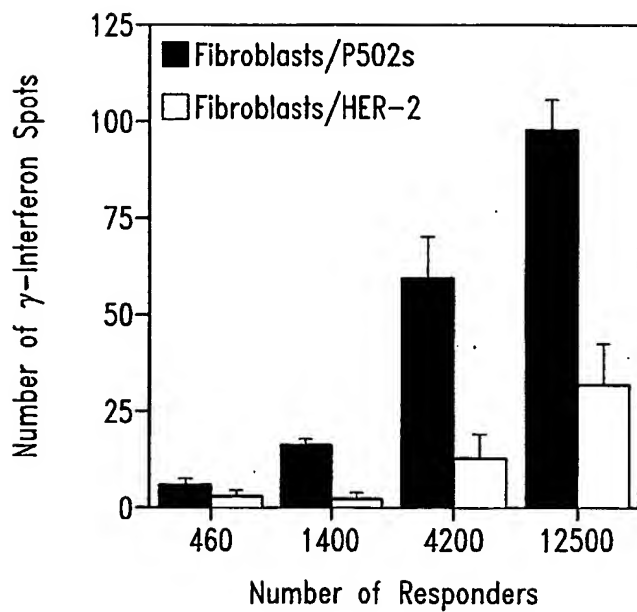
17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;
 - (b) administering to the patient an effective amount of the proliferated T cells,
- and thereby inhibiting the development of a cancer in the patient.

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*Fig. 1*

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*Fig. 2A**Fig. 2B*

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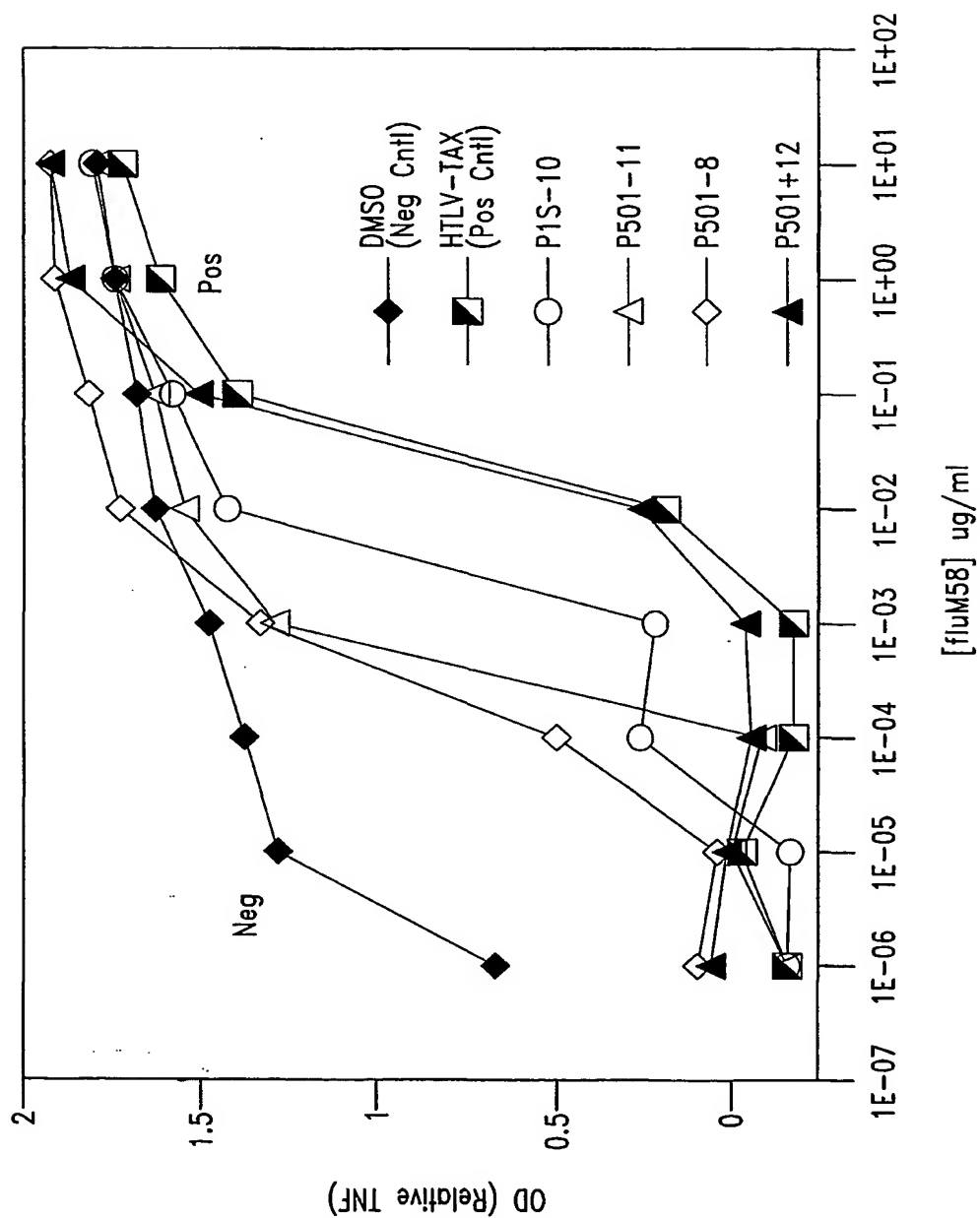
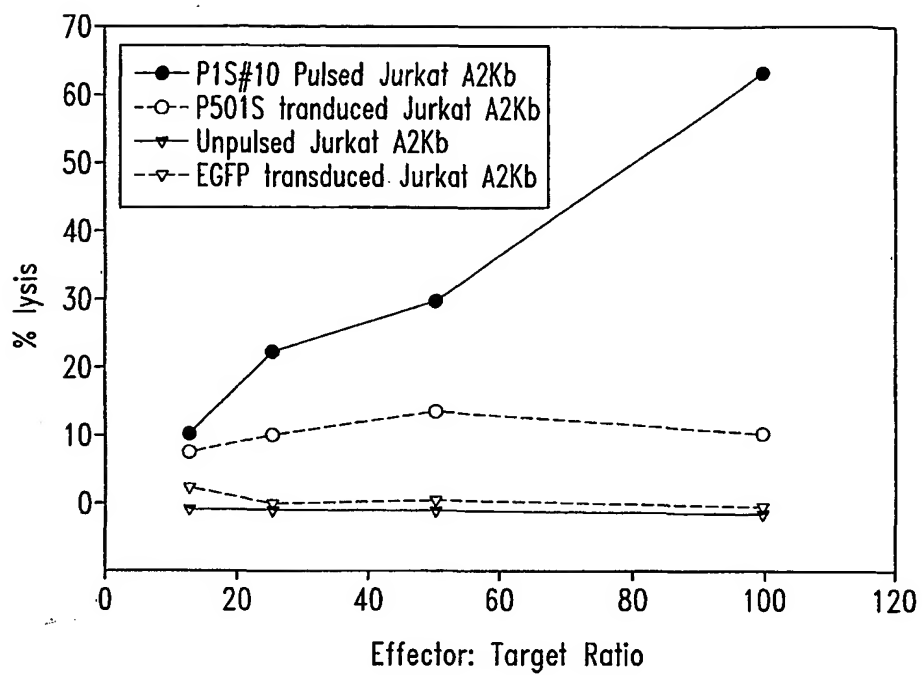
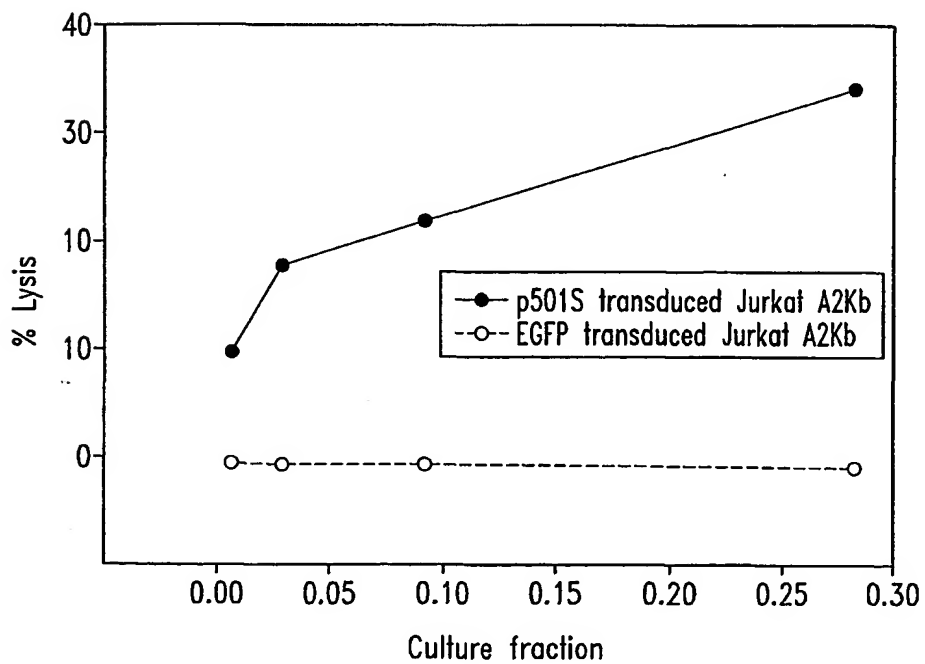
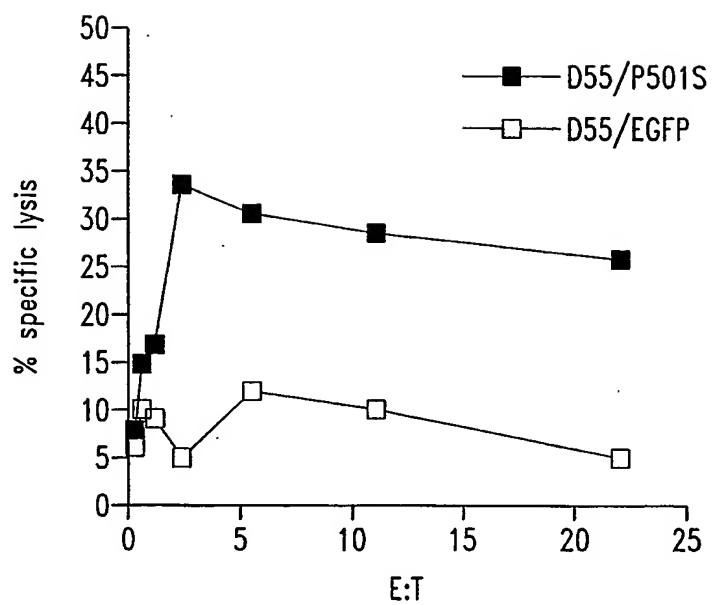
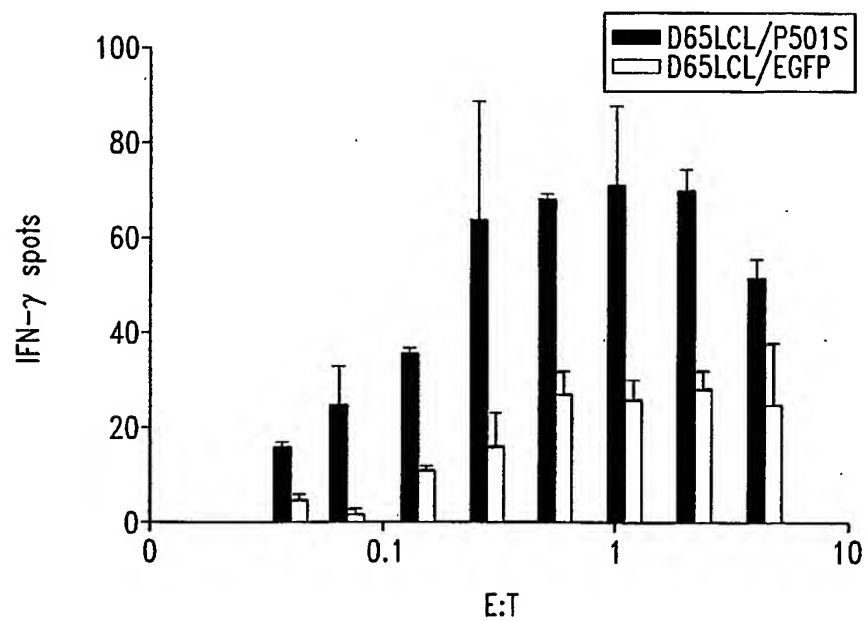


Fig. 3

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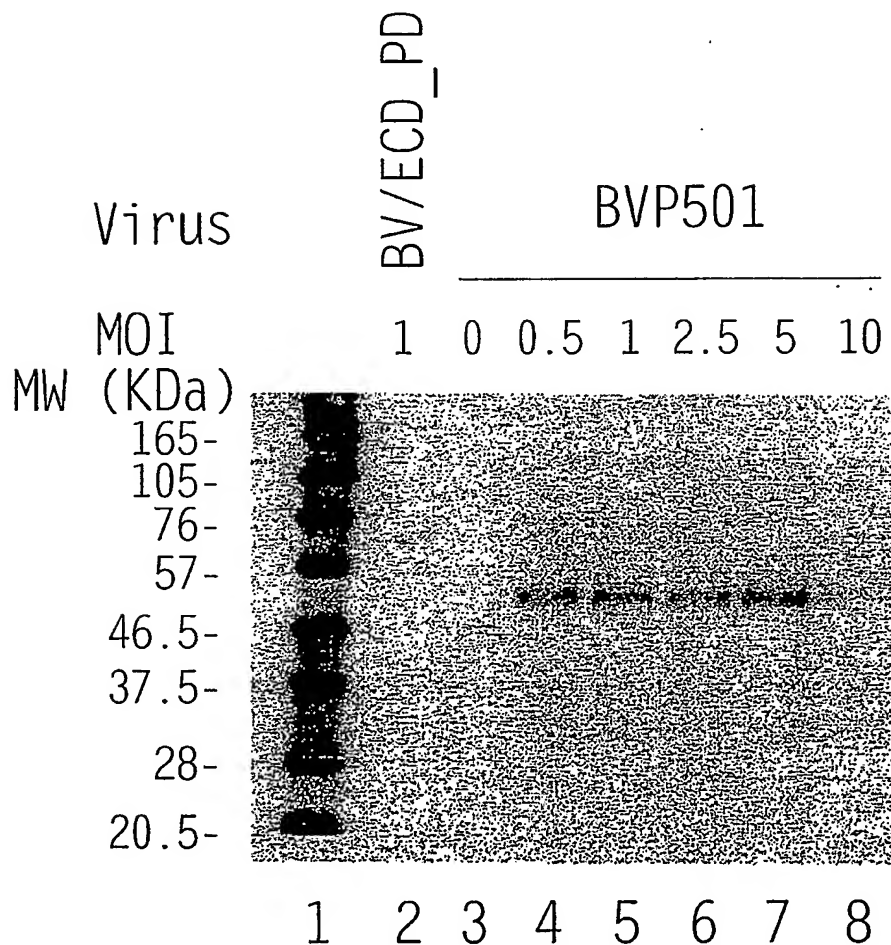
*Fig. 4**Fig. 5*

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*Fig. 6A**Fig. 6B*

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Expression of P501S
by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD_PD (lane2), without virus (lane3), or with recombinant baculovirus for P501 at different MOIs (lane 4-8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

FIGURE 8. Mapping of the epitope recognized by 10E3-G4-D3

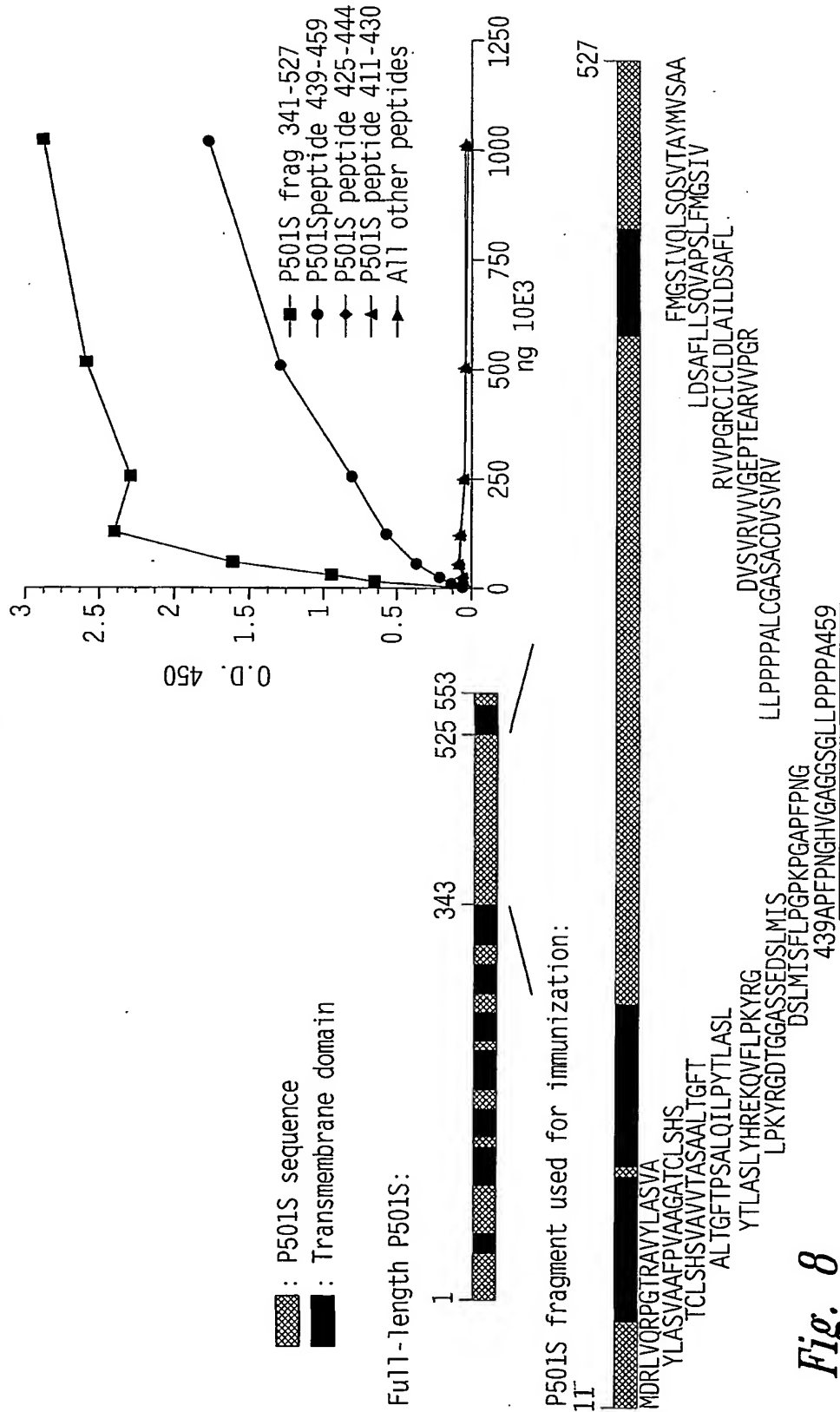


Fig. 8

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Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

MVQRLWVSRLLRHRK AQLLLVNLLTFGLEVCLAAGIT YVPLLLEVGVEEEKFM
TMVLGIGPVLGLVCYPLLGSAS

DHWRGRYGRRRP FIWALSGILLSLFLIPRAGWL AGLLCPDPRPLE LALLILGVGLLDFCGQVCFTPL

EALLSDLFRDPDHCRQ AYSVYAFMISLGGCLGYLLPAI DWDTSALAPYLGTQEE

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Underlined sequence: Predicted transmembrane domain; **Bold sequence**:
Predicted extracellular domain; *Italic sequence*: Predicted intracellular
domain. Sequence in bold/underlined: used generate polyclonal rabbit
serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon
(1998) Principles Governing Amino Acid Composition of Integral Membrane
Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

Fig. 9

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Genomic Map of (5) Corixa Candidate Genes

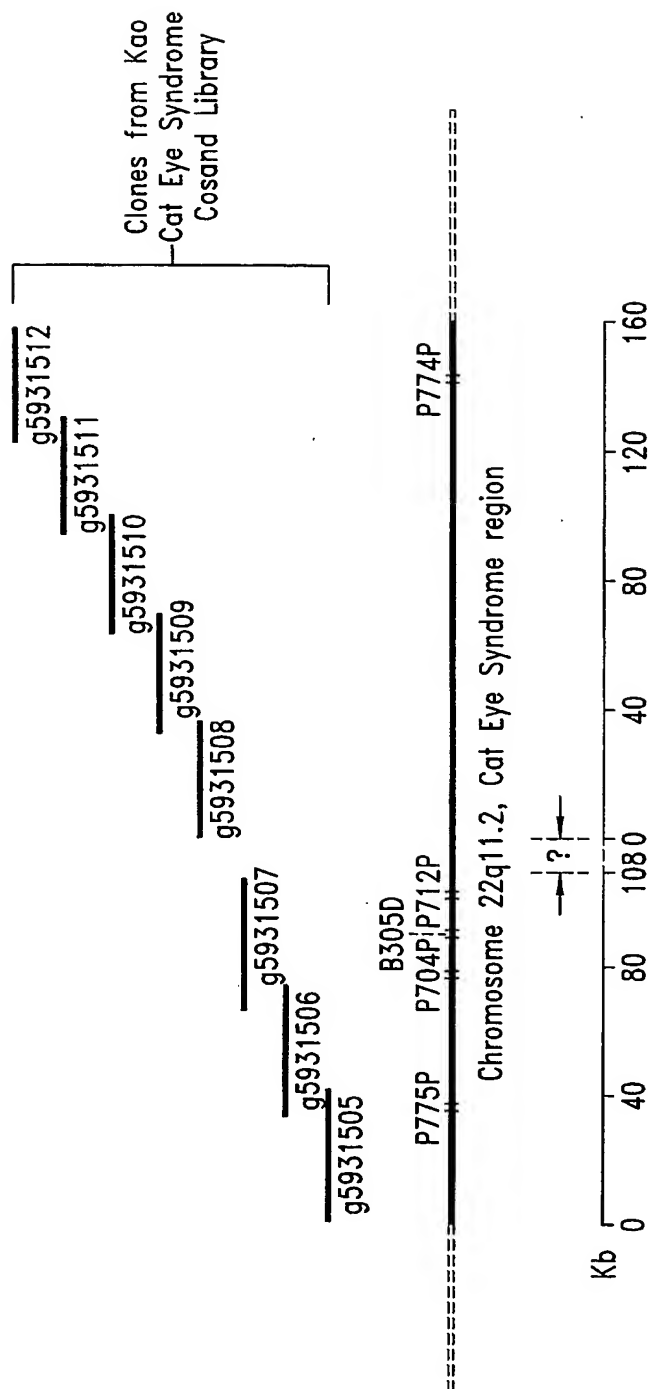


Fig. 10

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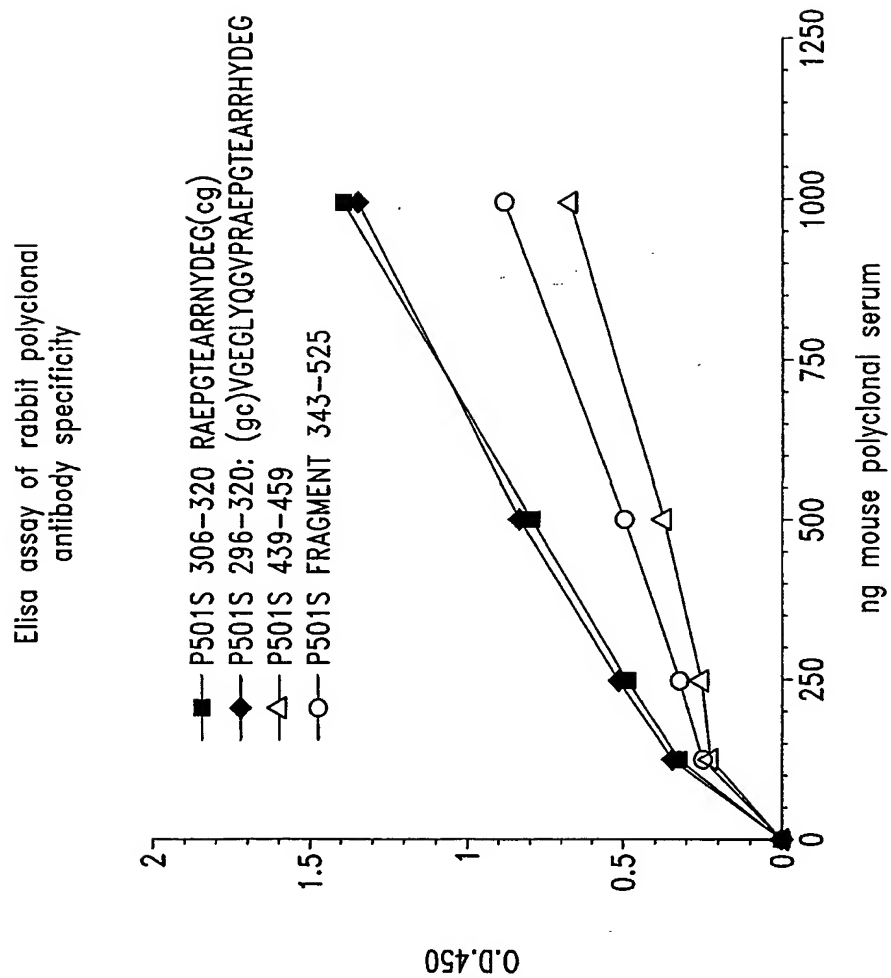


Fig. 11

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Fig. 12A (1)

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Fig. 12A (2)

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Fig. 12A (3)

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Fig. 12B

SEQUENCE LISTING

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 Xu, Jiangchun
 Dillon, Davin C.
 Mitcham, Jennifer L.
 Harlocker, Susan L.
 Yuqui, Jiang
 Kalos, Michael D.
 Fanger, Gary R.
 Retter, Marc W.
 Stolk, John A.
 Day, Craig H.
 Vedvick, Thomas S.
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 Li, Samuel
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cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt      120
ggtttgctcc acagatttca gagcattgac cgtagtatac cccgggtcgt gtagcggtga      180
aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaata gtggggacag      240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga      300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg      360
gaagtatgta ggaattgaag attaataccg cgtagtcggt gttctcctag gttcaatacc      420
attgggtggc aattgatatt atggtaaggg gagggatcgt tgaactcgtc tgttatgtaa      480
aggatncctt ngggatggga aggcnatnaa ggactangga tnaatggcgg gcangatatt      540
tcaaacngtc tctanttcct gaaacgtctg aaatgttaat aanaattaan tttngttatt      600
gaatnttng gaaaagggct tacaggacta gaaaccaaat angaaaanta atnntaangg      660
cnttatcntn aaagtnata accnctccta tnatccacc caatngnatt cccacncnn      720
acnattggat nccccanttc canaaanggc cccccccgg tgnannccnc cttttgttcc      780
cttnantgan ggttattcnc ccctngcntt atcanc      817

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<210> 8
<211> 799
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

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<400> 8
catttcggg tttactttct aaggaaagcc gagcgaagc tgctaactgt ggaatcggtg      60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt      120
ctgaagcgca cgtcccgaaa ggtggacttg gcactgaaac agctgggaca catcccgag      180
tacgaacagc gcctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtcctgggg      240
tgggtggccg angcctganc cgctctgcct tgctgcccc angtggggccg ccacccctg      300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac cccacangg      360

```

```

ggatthttgct cctanantaa ggctcatctg ggctcggcc cccccacctg gttggccttg 420
tctttgangt gagcccatg tccatctggg ccactgtcng gaccaccttt ngggagtgtt 480
ctccttacaa ccacannatg cccggctcct cccggaaacc antcccancc tngaaaggat 540
caagncctgn atccactnnt nctanaaccg gccnccnccg cngtggaacc cnccttntgt 600
tccttttctn tnagggttaa tnnccgcttg gccttnccan ngctcctncc nttttccnnt 660
gttnaaattg ttangcnccc nccnntcccn cncnncnccn cccgaccncc annttnnann 720
ncctgggggt nccnncngat tgaccenncc nccctntant tgctntnggg nncnntgccc 780
ctttccctct nggganncg 799

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<210> 9
<211> 801
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 9
acgccttgat cctcccaggc tgggactggt tctgggagga gccgggcatg ctgtggtttg 60
taangatgac actcccaaag gtggtcctga cagtggccca gatggacatg gggctcacct 120
caaggacaag gccaccagggt gcgggggccc aagccacat gatccttact ctatgagcaa 180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggaccang 240
cagggtcatg ggttgtngnc caactggggg ccncaacgca aaanggcncg gggcctcngn 300
cacccatccc angacgggc tacactnctg gacctccnc tccaccactt tcatgcgctg 360
ttcntaccg cgnatntgtc ccantgttt cngtgccnac tccancttct nggacgtgcg 420
ctacatacgc cggantcnc nctcccgtt tgctccctatc cagtnccan caacaaattt 480
cncntantg caccnattcc cacntttnc agntttccnc nncngcttc cttntaaaag 540
ggttgancgc cggaataatc ccaaaagggg gggggccngg taccacactn cccctnata 600
gctgaantcc ccatnaccnn gntcnatgg anccntccnt ttttaannacn ttctnaactt 660
gggaanancc ctgncnctn ccccnnttaa tccnccctg cnangnnct ccccnntcc 720
ncccnntng gcntntnann cnaaaaaggc ccnnnancaa tctcctnncc cctcanttgc 780
ccanccctgc aaatcggccn c 801

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<210> 10
<211> 789
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

```

```

<400> 10
cagtctatnt ggccagtgtg gcagctttcc ctgtggtgc cggtgccaca tgctgtccc 60
acagtgtggc cgtgttgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc 120
agatccctgc ctacacactg gcctccctct accaccggga gaagcaggtg ttccctgccca 180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttccctgc 240
caggccctaa gcctggagct ccctcccta atggacacgt ggtgctgga ggcagtggcc 300
tgctccacc tccaccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg 360
tggtgggtga gccaccgan gccagggtgg ttccgggccc gggcatctgc ctggacctgc 420
ccatccctga tagtgcttcc tgctgtccca ngtgcccca tccctgttta tgggctccat 480
tgtccagctc agccagtctg tcaactgccta tatggtgtct gccgcaggcc tgggtctggt 540
cccatttact ttgtacaca ggtantattt gacaagaacg anttggccaa atactcagcg 600
ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc 660
tcctgttaac cccatggggc tgccggcttg gccgccaatt tctgttgctg ccaaantnat 720

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gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtnng 780
 ggngttccc 789

<210> 11
 <211> 772
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(772)
 <223> n = A,T,C or G

<400> 11
 cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60
 tttgttaaataaataagtttaaatattttaa tgccctgtgtc tctgtgatgg caacagaagg 120
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180
 tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata 240
 actttcatat gttcaaattcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300
 ctacattaaa cgaagctgca ggtaagggg cttanagatg ggaaaccagg tgactgagtt 360
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420
 ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc 480
 ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana 540
 aactggggaa aaaagaaaag gacgccccan ccccagctg tgcanctacg cacctcaaca 600
 gcacagggtg gcagcaaaaa aaccacttta ctttggcaca acaaaaaact ngggggggca 660
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720
 ggcccnccac ccnnaatntt gctgggaaat ttttctccc cttaattntt tc 772

<210> 12
 <211> 751
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 12
 gcccgaattc cagctgccac accacccacg gtgaactgcat tagttcggat gtcatacaaa 60
 agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggg gcaggtttca 120
 ttggctgtgt tggtagctt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
 aagtanggtg agtctcaaaa atccgtatag ttggtgaagc cacagcactt gagcccttcc 240
 atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
 ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac 360
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420
 acacttgctc tcagtcttan caccatgca gccntgaaa accaananca aagaccacna 480
 cncggctgc gatgaagaaa tnaacccttg ttgacaaact tgcattggcac tggganccac 540
 agtggccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg 600
 ccaacagggg ctgccccacn cncnnaacga tgancnatt gnacaagatc tncntggtct 660
 tnatnaacnt gaacctgcn tngtggctcc tgttcaggnc cnggcctga cttctnaann 720
 aangaactcn gaagncccca cngganannc g 751

<210> 13
 <211> 729
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(729)
 <223> n = A,T,C or G

<400> 13
 gagccaggcg tccctctgcc tgcccactca gtggcaaacac ccgggagctg ttttgcctt 60
 tgtggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc 120
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180
 ctgtgtgggtg cagccctggt ggccagtgggc atctgggtgt caatcgatgg ggcatccttt 240
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300
 ctcatcgag ccggcggtgt ggtcttagct ctagggttcc tgggctgcta tgggtgctaag 360
 actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct 420
 gaggttgcaa tgctgtggtc gccttgggtg acaccacaat ggctgagcac ttcctgacgt 480
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc cagggaanact tcactcaagt 540
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatatt 600
 gaagantcac ctacttcaaa gaaaanagt cctttccccc atttctgttg caattgacaa 660
 acgtccccaa cacagccaat tgaaaacctg caccacaacc aaanggggtcc ccaaccanaa 720
 attnaaggg 729

<210> 14
 <211> 816
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(816)
 <223> n = A,T,C or G

<400> 14
 tgctcttcct caaagttggt cttgttgcca taacaaccac cataggtaaa gcgggcgcag 60
 tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgcagag tcctgtgtct 120
 ggcaaggtcca cgcagtgcc ttgtcactg gggaaatgga tgcgctggag ctctgcaaag 180
 ccactcgtgt atttttcaca ggcagcctcg tcgcacgcgt cggggcagtt gggggtgtct 240
 tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaaactg ggtgggctga 300
 cangtgccag agcacactgg atggcgctt tccatggnan gggccctgng ggaaagtccc 360
 tganccccc anctgcctct caaangcccc accttgacac ccccgacagg ctagaatgga 420
 atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt 480
 gcanatctgc tccngggggg tcntantacc ancggtggaa aagaacccca ggcngcgaac 540
 caancttggt tggatnoga gcnataatct nctnttctgc ttggtggaca gcaccantna 600
 ctgtnnanct ttagnccntg gtctctntgg gttgnncttg aacctaatcn ccnntcaact 660
 gggacaaggt aantngccnt cctttnaatt cccnancntn cccctggtt tggggttttn 720
 cncnctcta cccagaaan nccgtgttcc ccccaacta ggggcnaaa ccnntnttc 780
 cacaaccctn cccacccac gggttcngnt ggttng 816

<210> 15
 <211> 783
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(783)
 <223> n = A,T,C or G

<400> 15
 ccaaggcctg ggcaggcata nacttgaagg tacaaccca ggaaccctg gtgctgaagg 60

atgtggaaaa	cacagattgg	cgcctactgc	ggggtgacac	ggatgtcagg	gtagagagga	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtgactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcact	gtgctgtcca	240
ccaagcagac	agaagactac	tgcctcgcac	ccaacaangt	gggtcgctgc	cggggctctt	300
tcccacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttcggt	tatggaggct	360
gcttgggcaa	caagaacaac	taccttcggg	aagaagagtg	cattctancc	tgtcnggggtg	420
tgcaagggtg	gcctttgana	ngcanctctg	gggtcangc	gactttcccc	cagggcccct	480
ccatggaaag	gcgccatcca	ntgttctctg	gcacctgtca	gcccaccag	ttccgctgca	540
ncaatggctg	ctgcatcnac	antttcctng	aattgtgaca	acacccccca	ntgcccccaa	600
ccctcccaac	aaagcttccc	tgttnaaaaa	tacnccantt	ggcttttnac	aaacncccg	660
cncctcctnt	ttccccnntn	aacaaagggc	nctngcnttt	gaactgcccn	aaccnnggaa	720
tctnccnngg	aaaaantncc	ccccctggtt	cctnnaancc	cctccnnaa	anctncccc	780
ccc						783

<210> 16
 <211> 801
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(801)
 <223> n = A,T,C or G

<400> 16						
gccccaatc	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttgg	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatggg	gaaaggcact	gttctctttg	180
aagttagggg	agtccctcaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
atgggtgtgt	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	gaagtgtc	gccattgtg	tgtacaccaa	ggcgaccaca	360
gcagctgcaa	cctcagcaat	gaagatgagg	aggaggatga	agaagaacgt	cncgagggca	420
cacttgctct	cgtctttagc	accatagcag	cccangaaac	caagagcaaa	gaccacaacg	480
ccngctgcga	atgaaagaaa	ntaccacgt	tgacaaactg	catggccact	ggacgacagt	540
tgccccgaan	atcttcagaa	aagggatgcc	ccatcgattg	aacacccana	tgcccactgc	600
cnacagggct	gcncncncn	gaaagaatga	gccattgaag	aaggatcntc	ntggtcttaa	660
tgaactgaaa	ccttgcatgg	tggcccctgt	tcagggctct	tggcagtga	ttctganaaa	720
aaggaaacng	ntnagcccc	ccaaangana	aaacaccccc	gggtgttgcc	ctgaattggc	780
ggccaaggan	ccctgccccn	g				801

<210> 17
 <211> 740
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(740)
 <223> n = A,T,C or G

<400> 17						
gtgagagcca	ggcgtccctc	tgcctgccca	ctcagtgcca	acacccggga	gctgttttgt	60
cctttgtgga	gcctcagcag	ttccctcttt	cagaactcac	tgccaagagc	cctgaacagg	120
agccaccatg	cagtgcctca	gcttcattaa	gaccatgatg	atcctcttca	atttgctcat	180
ctttctgtgt	ggtgcagccc	tgttggcagt	gggcactctg	gtgtcaatcg	atggggcatc	240
ctttctgaag	atcttcgggc	cactgtcgtc	cagtgccatg	cagtttgtca	acgtgggcta	300
cttctctatc	gcagccggcg	ttgtggctct	tgtcttgggt	ttcctgggct	gctatgggtc	360
taagacggag	agcaagtgtg	ccctcgtgac	gttcttcttc	atcctcctcc	tcattctcat	420

tgctgaagtt	gcagctgctg	tggtcgctt	ggtgtacacc	acaatggctg	aaccattcct	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	ttcccaggaa	aaattcactc	540
aantntggaa	caccnccatg	aaaagggctc	caatttctgn	tggtttcccc	aactataccg	600
gaattttgaa	agantcnccc	tactttccaaa	aaaaaanant	tgcttttnc	ccntttctgt	660
tgcaatgaaa	acntcccaan	acngccaatn	aaaacctgcc	cnncnaaaaa	ggntcncaaa	720
caaaaaaant	nnaagggttn					740

<210> 18

<211> 802

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(802)

<223> n = A,T,C or G

<400> 18

ccgctgggtt	cgctgggtcca	gngnagccac	gaagcacgtc	agcatacaca	gcctcaatca	60
caaggtcttc	cagctgccgc	acattacgca	gggcaagagc	ctccagcaac	actgcatatg	120
ggatacactt	tacttttagca	gccaggggtga	caactgagag	gtgtcgagag	ttattcttct	180
gagcctctgt	tagtgagga	agattccggg	cttcagctaa	gtagtcagcg	tatgtcccat	240
aagcaaacac	tgtgagcagc	cggaaggtag	aggcaaatgc	actctcagcc	agctctctaa	300
cattgggcat	gtccagcagt	tctccaaaca	cgtagacacc	agnggcctcc	agcacctgat	360
ggatgagtgt	ggccagcgct	gcccccttgg	ccgacttggc	taggagcaga	aattgtcctt	420
ggttctgccc	tgtcaccttc	acttcgcgac	tcatacttgc	actgagtgtg	ggggacttgg	480
gctcaggatg	tccagagacg	tggttccggc	ccctcnctta	atgacaccgn	ccanncaacc	540
gtcggctccc	gccgantgng	tctgtcgtnc	ctgggtcagg	gtctgctggc	cnctacttgc	600
aanccttcgtc	nggcccatgg	aattcacenc	accggaactn	gtangatcca	ctnnttctat	660
aaccggncgc	caccgcnnnt	ggaactccac	tcttnttnc	tttacttgag	ggttaagggtc	720
acccttncg	ttaccttgg	ccaaaccntn	ccntgtgtcg	anatngtnaa	tcnggncna	780
tnccancnc	atangaagcc	ng				802

<210> 19

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 19

cnaagcttcc	aggtnacggg	ccgcnaancc	tgaccnagg	tancanaang	cagncngcgg	60
gagcccaccg	tcacngngng	gngtctttat	nggagggggc	ggagccacat	cnctggacnt	120
cntgaccca	actcccnc	ncncantgca	gtgatgagtg	cagaactgaa	ggtnacgtgg	180
caggaaceaa	gancaaannc	tgctccnntc	caagtgcgcn	nagggggcgg	ggctggccac	240
gcncatccnt	cnagtgtctn	aaagccccnn	cctgtctact	tgtttgaga	acngcnnga	300
catgccca	ggtanataac	nggcngagag	tnantttgcc	tctcccttcc	ggctgcgc	360
cgngtntgct	tagnggacat	aacctgacta	cttaactgaa	cccnngaate	tnccnccct	420
ccactaagct	cagaacaaaa	aacttcgaca	ccactcantt	gtcacctgnc	tgctcaagta	480
aagtgtaccc	catncccaat	gtntgctnga	ngctctgncc	tgcnttangt	tcggtcctgg	540
gaagacctat	caattnaagc	tatgtttctg	actgcctctt	gctccctgna	acaancnacc	600
cnncnntcca	agggggggnc	ggcccccaat	ccccccaacc	ntnaattnan	tttancccn	660
ccccnggcc	cggcctttta	cnancntcnn	nnaacnggna	aaaccnnngc	tttncccaac	720
nnaatccncc	t					731

<210> 20
 <211> 754
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(754)
 <223> n = A,T,C or G

<400> 20
 tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
 caacccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120
 annttaaatt aaatnttntt tggnggnnna anccnaatgt nangaaagt naaccanta 180
 tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
 aaatngttna nggaaaaccc aanttctcnt aagggtgttt gaaggntnaa tnaaaanccc 300
 nnccaattgt ttttngccac gcctgaatta attggnntcc gntgttttcc nttaaaanaa 360
 ggnnanccccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntccggg 480
 ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540
 ccaggtgag nntnggggtt ncccccccc canggccct ctcgnaaggt tgggggtttg 600
 ggggcctggg atttntttt cctntttnc tcccccccc ccngganag aggttngngt 660
 tttgntcnc ggcccnccn aaganccttn ccganttnan ttaaatecnt gcctnggcga 720
 agtccnttgn agggntaaan ggccccctnn cggg 754

<210> 21
 <211> 755
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(755)
 <223> n = A,T,C or G

<400> 21
 atcancat gacccnaac nngggaccnc tcancggnc nnncnaccnc cggccnatca 60
 nngtnagnnc actncnttn natcacnccc cnccnactac gcccnananc cnacgcnta 120
 nncanattcc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180
 ccagctgtcc nanaangcct nnnatacnng nnnatccaat ntgnancctc cnaagtattt 240
 nncnncanatt gattttcctn anccgattac ccntncccc tanccctcc cccccaacna 300
 cgaaggcnct ggncnaagg nngcgncc cgcctagntc ccnncaagt cncncccta 360
 aactcancn nattacnccg ttcntgagta tcaactcccg aatctcacc tactcaactc 420
 aaaaanactn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
 ttagnggtcc ntnaancntc ctaatacttc cagctcncct tcnccaattt ccnaanggt 540
 ctttcngaca gcatntttt gttcccnntt ggggtcttan ngaattgcc ttcntngaac 600
 gggctcntct tttccttcgg ttancctggn ttcnccggc cagttattat tcccnnttt 660
 aaattcntnc cntttanttt tggcnttcna aaccccgcc cttgaaaacg gccccctggt 720
 aaaagggtgt ttganaaaa ttttgtttt gttcc 755

<210> 22
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 22

tttttttttt	tttttangtg	tngtcgtgca	ggtagaggct	tactacaant	gtgaaahacgt	60
acgctnggan	taangcgacc	cgantttctag	gannncnccct	aaaatcanac	tgtgaagatn	120
atcctgnnna	cgggaanggtc	accggnggat	nntgctaggg	tgncnctcc	cannncnttn	180
cataactcng	nggccctgcc	caccaccttc	ggcggccng	ngnccgggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	nccccnncng	accngggcga	tccggggtn	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttaccct	nnacaagcca	360
cngccttcta	nccncngccc	cccctccant	nngggggact	gccnanngt	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgctcgant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	gcccctaccc	ttcgctncgg	nncacccttc	ccgacnanga	nccgctccc	540
cncnncgnng	cctcncctcg	caacacccgc	ntctntcngt	ncggnnnccc	ccccaccgc	600
nccctcncnc	ngnccgnancn	ctcncncncc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggnggacnng	nagcncnttc	gcnccgccgn	gcgncnccct	cgccncngaa	720
ctnctcngg	ccantnncgc	tcaanccnna	cnaaacgccg	ctgcgcggcc	cgnagcgncc	780
ncctcncga	gtcctcccgn	cttccnacc	angnnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

gcgcaaaacta	tacttgcgtc	gnactcgtgc	gcctcgtcnc	tcttttctctc	cgcaaccatg	60
tctgacnanc	ccgatnnggc	ngatatcnan	aagntcganc	agtccaaact	gantaacaca	120
cacacncnan	aganaaatcc	notgccttcc	anagtanaacn	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgcgcgcca	atntgtcnc	gtttattntn	ccagctcnc	240
ctnccnacc	taentctten	nagctgtcnn	accctngtn	cgnaccccc	naggtcggga	300
tgcgggtttn	nntgaccng	cnnccctcc	ccccctccat	nacgancnc	ccgcaccacc	360
nanngcncgc	nceccgnct	cttcgcnc	ctgtcctntn	cccctgtngc	ctggcncngn	420
accgcattga	ccctcgccnn	ctncnngaaa	ncgnanacgt	ccgggttggn	annancgctg	480
tgggnnngcg	tctgcncgc	gttccttccn	ncncttcca	ccatcttnt	tacnnggtct	540
ccnccgcntc	tcnnncacnc	cctgggacgc	tntcctntgc	cccccttnac	tccccccctt	600
cgncgtgncc	cgnccccacc	ntcatttnca	nacgntcttc	acaannncct	ggntnnctcc	660
cnancngncn	gtcanccnag	ggaagggngg	ggnnccnntg	nttgacgttg	nggngangtc	720
cgaanantcc	tcnccntcan	cnetaccct	cgggcgnnct	ctcngttnc	aacttancaa	780
ntctcccccg	ngngcncntc	tcagcctcnc	ccnccccnct	ctctgcantg	tntctgtctc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcatgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggtcnta	60
------------	------------	------------	------------	------------	------------	----

12

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nctgncttcc tgtgtcaaat gtatacnaa tanatatgaa tctnatntga caaganngta 120
tcntncatta gtaacaantg tnntgtccat cctgtcngan canattccca tnnattncgn 180
cgcaattcn cn gncantatn taatngggaa ntcnnntnnn ncaccnncat ctatcntncc 240
gcnccttgac tgganagagat ggatnanttc tnntntgacc nacatgttca tcttggattn 300
aananccccc cgcnngccac cggttngnng cnagccnntc ccaagacctc ctgtggaggt 360
aacctgcgtc aganncatca aacntgggaa acccgcnnc angtnnaagt ngnnncanan 420
gatcccgctc aggnntnacc atcccttcnc agcgccccct ttngtgcctt anagnngnagc 480
gtgtccnanc cnetcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc 540
gaaccccta gggggantna tncaaanccc caggattgtc cncncangaa atcccnanc 600
ccnccctac ccncttttg gacngtgacc aantcccga gtnccagtc gcccnngctc 660
ccccaccgt nncntgggg ggggtgaanct cngnntcanc cngncgaggn ntcgnaagga 720
accggnccn ggnccgaanng ancntcnga agngccnct cgtataacc cccctcncca 780
nccnacngnt agntcccccc cngggtnccg aang 815

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<210> 25
<211> 775
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(775)
<223> n = A,T,C or G

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```

<400> 25
ccgagatgtc tgcctcgtg gccttagctg tgctcgcgt actctctctt tctggcctgg 60
aggctatcca gcgtactcca aagattcagg ttactcacg tcatccagca gagaatggaa 120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact 180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg 240
actggctctt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtag 300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca 360
tgtaagcagn cncatggaa gtttgaagat gccgatttg gattggatga attccaaatt 420
ctgcttgctt gcnttttaat antgatatgc ntatacacc taccctttat gnccccaaat 480
tgtaggggtt acatnantgt tcncntngga catgatctt cttataant ccncnttcg 540
aattgcccg cncncngtn ngaatgttcc cnaaccacg gttggctccc ccaggtcncc 600
tcttacggaa gggcctgggc cnccttncaa ggttggggga accnaaaatt tcncntntgc 660
ccncccncca cmtcttgng nncncanttt ggaaccctt cnattcccct tggcctcnna 720
nccttnncta anaaaacttn aaancgtngc naaannttn acttcccccc ttacc 775

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<210> 26
<211> 820
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(820)
<223> n = A,T,C or G

```

```

<400> 26
anattantac agtgaatct tttccagag gtgtgtanag ggaacggggc ctagaggcat 60
cccanagata ncttatanca acagtgcctt gaccaagagc tgctgggcac atttctgca 120
gaaaagggtg cgtcccat cactcctcct ctcccatagc catccagag gggtagtag 180
ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca 240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg ggggtggcana nganagccta 300
nctgaggggt cacactataa acgttaacga ccnagatnan cactgcttc aagtgcaccc 360
ttcctacctg acnaccagn accnnnaact gcngcctggg gacagcnctg ggancagcta 420
acnnagcact cacctgcccc cccatggcgg tncgcntccc tggctctgnc aagggaagct 480

```

```

cctgttgga attncgggga naccaaggga nccccctcct ccancgtgtga aggaaaaaann 540
gatggaattt tnccttcccg gccnntcccc tcttcttta cacgccccct nntactcntc 600
tccctctntt ntectgnenc acttttnacc ccnnnatttc ccttnattga tcggannctn 660
ganattccac tnnccgctnc cntcnatcng naanacnaaa nactntctna ccnnggggat 720
gggnnccctcg ntcacccctct ctttttctct accnccnntt ctttgcctct ccttngatca 780
tccaacntc gntggccntn cccccccnnn tcttttnccc 820

```

<210> 27

<211> 818

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(818)

<223> n = A,T,C or G

<400> 27

```

tctgggtgat ggcctcttcc tcctcaggga cctctgactg ctctgggcca aagaatctct 60
tgfttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120
ctgoggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggagc 180
ctgctgagca cttccgcccc tcaccctgcc cagccctgc catgagctct gggctgggtc 240
tccgcctcca gggttctgct cttccangca ngccancaag tggcgtggg ccacactggc 300
ttcttctctg cccttccctg gctctgantc tctgtcttcc tgtcctgtgc angcnccttg 360
gatctcagtt tccctcncctc anngaactct gtttctgann tcttcantta actntgantt 420
tatnacnan tggntgtnc tgtcnnactt taatgggcn gaccggctaa tccctccctc 480
nctcccttcc anttcnnnna accngcttnc cntctctcc cntancccg ccngggaanc 540
ctcctttgcc ctnaccangg gccnnnaccc ccctnnctn ggggggcnng gtnnctnenc 600
ctgntnnccc cncctcnnt tncctctgcc cncnncgcn nngcannttc ncngtcccn 660
tnnctcttcn ngntcgnaa ngntcnctn tnnnnngcn ngntnntcn tccctctnc 720
cnnntgnang tnnntnnnc ncngnncccc nnnnnnnnn nggnntnnn tctnncngc 780
ccnnccccc ngnattaagg cctccnntct ccggccnc 818

```

<210> 28

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 28

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aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg 60
tcccaacatg anggtgnngt tctcttttga angagggttg ngtttttann ccnggtgggt 120
gattnaaccc cattgtatgg agnnaaagg ntttagggat ttttcggctc ttatcagtat 180
ntanattcct gtnaatcgga aaatnatntt tcnnccggaa aatnttgctc ccatccgnaa 240
attnctcccg ggtagtgcatt nttinggggn cngccangtt tcccaggctg ctanaatcgt 300
actaaagntt naagtggan tncaaatgaa aacctnnac agagnatccn taccgactg 360
tnnnttncct tcgcctntg actctgcnn agccaatac ccnngngnat gtcncccn 420
nnngcgnenc tgaannnnn tcgnggctnn gancatcang gggtttcgca tcaaaagcnn 480
cgtttcncat naaggcactt tngcctcatc caaccnctng ccctcncca tttngccgtc 540
nggttcnct acgctnntng cncctnnntn ganattttnc ccgcctnngg naancctcct 600
gnaatgggta gggntctntc ttttnaccnn gnggtntact aatcnctnc acgcntnctt 660
tctcnacccc ccccttttt caatcccanc ggcnaatggg gtctccccnn cgangggggg 720
nnnccannnc c 731

```

14

<210> 29
 <211> 822
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(822)
 <223> n = A,T,C or G

<400> 29
 actagtccag tgtggtggaa ttccattgtg ttgggggncnc ttctatgant antnttagat 60
 cgctcanacc tcacancctc ccnaccnangc ctataangaa nannaataga nctgtncnnt 120
 atntntacnc tcatanncct cnnnaccacac tccctcttaa cccntactgt gcctatngcn 180
 tnnctantct ntggccgectn cnanccaccn gtggggccnac cncnngnatt ctcnatctcc 240
 tcnccatntn gcctananta ngtnccatacc ctatacctac nccaatgcta nnnctaancn 300
 tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc 360
 tactctgact cccacngect annnattagc ancntccccc nacnatntct caaccaaatc 420
 ntcaacaacc tatctantctg ttcnccaacc nttncctccg atccccnnac aacccccctc 480
 ccaaataccc nccacctgac ncctaaccn caccatcccg gcaagccnan ggncatttan 540
 ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctcccctaana 600
 aatnctcctn naatttactn ncanntccat caanccacn tgaaacnnaa cccctgtttt 660
 tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccnctnc 720
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780
 canatcctat cccttanttn ggggnccctt ncccnngggc cc 822

<210> 30
 <211> 787
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(787)
 <223> n = A,T,C or G

<400> 30
 cggccgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120
 gtctgcaagg tttgatgtct gaagtcgtgg agtgtggctt ggagctccto atctacatna 180
 gctggaagcc ctggaggggc tctctcgcca gcctccccct tctctccacg ctctccangg 240
 acaccagggg ctccaggcag cccattatc ccagnangac atgggtgttc tccacgcgga 300
 cccatggggc ctgnaaggcc aggggtctcct ttgacaccat ctctcccgtc ctgcctggca 360
 ggccgtggga tccactantt ctanaacggn cggcaccncg gtgggagctc cagcttttgt 420
 tccnttaat gaagggttaat tgcncgctt gcgtaatcat nggtcanaac tntttcctgt 480
 gtgaaattgt ttntccctc ncnattccnc ncnacatacn aaccgggaan cataaagtgt 540
 taaagcctgg gggtngecctn nngaataaac tnaactcaat taattgcgtt ggctcatggc 600
 ccgctttccn ttcnngaaaa ctgtcntccc ctgcnttnnt gaatcgcca cccccnggg 660
 aaaagcgggt tgcnttttng ggggntcctt ccncttcccc cctcnctaan ccctnccgct 720
 cggtcgttnc nggtngcggg gaanggnat nnnctccnc naagggggng agnnngntat 780
 ccccaaa 787

<210> 31
 <211> 799
 <212> DNA
 <213> Homo sapien

<220>

15

<221> misc_feature
 <222> (1)... (799)
 <223> n = A,T,C or G

<400> 31
 tttttttttt tttttttggc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac 60
 catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc 120
 aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct 180
 cccgcagggt gggggccacc agtccagggt tgggagcact acanggggtg ggagtgggtg 240
 gtggctggtg cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca 300
 ggggaccttc tgttctccca nggnaacttc nttnatctcn aaagaacaca actgtttctt 360
 cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca 420
 tatggttccg gcccacctct cccntcnaaa agtaattca ccccccccn cctctnttg 480
 cctgggccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg 540
 ntnatncn cctgaangcg ccaagttgaa aggccacgcc gtncnctc cccatagnan 600
 nttttnnct canctaatagc cccccnngc aacnatcaa tcccccccn tgggggcccc 660
 agcccanggc ccccgntcgg ggnnnccnng cncgnantcc ccagntctc ccantcngc 720
 ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnnncac 780
 ctgccccccc ccnnccgnng 799

<210> 32
 <211> 789
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (789)
 <223> n = A,T,C or G

<400> 32
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 ttttncnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac 120
 ggcaacaggc tccggcgcg cgggcgcgcg ccctacctgc ggtaccaa ntgcagcctc 180
 cgctcccgct tgatnttcc ctgcagctgc aggatgcctt aaaaacagggc ctgcggcctn 240
 ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc 300
 nattaggaat agtggnttta cccnccnccg ttggcncact ccccntggaa accacttntc 360
 gcggtccgg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt 420
 nccngccaca atcatnactc agactggcnc gggctggccc caaaaaan cnccaaaacc 480
 ggnccatgtc ttncgggggt tgcctgcnat tncatcacct cccgggcnca ncaggncaac 540
 ccaaaagtgc ttgnggccc caaaaaanct ccggggggnc ccagtttcaa caaagtcac 600
 ccccttggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnnctt 660
 tggngggcaa gntggntccc ccttcgggcc cccggtgggc ccnctctaa ngaaaacncc 720
 ntctnnnca ccatccccc nngnnacgnc tancaangna tccctttttt tanaaacggg 780
 cccccnccg 789

<210> 33
 <211> 793
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (793)
 <223> n = A,T,C or G

<400> 33
 gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg 60

16

```

aattcatggc tgttggagca atanaacccc agttctacga gctgctgac aaaggacttg 120
gactaaagt c tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana 180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg 240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca 300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac 360
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaatttt aaagcctggg ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaac acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncttccc gctttctcgc ttcctgaant ccttcccccc ggtctttcgg cttgcggcna 780
acggtatcna cct 793

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<210> 34

<211> 756

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(756)

<223> n = A,T,C or G

<400> 34

```

gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt 60
ancaagtgcg gggaanagct gggctgactc aagctagtgc ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtga catactggag 180
atcgggggccc aatggagcat cctacgcaan gacatccctt ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttcttg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggctgcc tggcgaanga catacanacc aatgtctaca tcnaccacca 420
gtgtccttga gcaatactga tgganggcag ctacncaaaa gtnttctctg ccnagggtaa 480
catccccgc cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn gggtgtctca gaaaggctnc aanaanatcc ttttcnctga aggccccggg 600
atnncntagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttnccct 660
ttactgaggg ttntatgccg cccttggcgt tatcatggtc acnccngttn cctgtgttga 720
aattnttaac cccccacaat tccacgcena cattng 756

```

<210> 35

<211> 834

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(834)

<223> n = A,T,C or G

<400> 35

```

ggggatctct anactnacct gnatgcatgg ttgtcgggtg ggtcgtgtc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggtc gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cncctctggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct cgggtgaactc gatgacnang ggcagctggg tgtgtntgat 240
aaantccanc angttctcct tggtgacctc cccttcaaaag ttgttccggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactgtt 360
ggaaactgat cccaaatggg atgtcatcca tcgcctctgc tgccctgcaa aaacttgctt 420
ggcncaaate cgactcccn tccttgaaag aagccnatca cccccctc cctggactcc 480

```

17

```

nncaangact ctnccgctnc ccntccnng caggggttggg ggcanncgg gcccntgcgc 540
ttcttcagcc agttcacnat nttcatcagc ccctctgcc gctgttntat tccttggggg 600
ggaanccgtc tctcccttc tgaannaact ttgaccgtng gaatagccgc gcntcncnt 660
acntnctggg cggggttcaa antccctccn ttgncnntcn cctcggggcca ttctggattt 720
nccnaacttt ttccttcccc cncccnccgg ngtttggnnt tttcatnggg ccccaactct 780
gctnttggcc antcccttg ggcntntan cnccccctnt ggtcccntng ggcc 834

```

```

<210> 36
<211> 814
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(814)
<223> n = A,T,C or G

```

```

<400> 36
cggncgcttt ccngccgcgc ccggtttcca tgacnaaggc tcccttcang ttaaatacnn 60
cctagnaAAC attaatgggt tgctctacta atacatcata cnaaccagta agcctgccc 120
naagccaac tcaggccatt cctaccaaag gaagaaaggc tggctctctc accccctgta 180
ggaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact 240
aatggaaaaa aaaaataaac aanagggttt gtctcatgg ctgccaccg cagcctggca 300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgcctt ttggacatca 360
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480
aggggangtc ntttncagtg gatctgcca anantaccn tatcatcnnt gaataaaaag 540
gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc 600
cttcgggtct gatccnaaag gaatgttcct ggggtccant cctcctttg ttncctacgt 660
tgtnttgga cctgctngn atnaaccaan tganatcccc ngaagcacc tncctctggc 720
atttganttt cntaaattct ctgcctacn nctgaaagca cnattccctn ggcnccnaan 780
gnggaactca agaaggtctn ngaaaaacca cncn 814

```

```

<210> 37
<211> 760
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(760)
<223> n = A,T,C or G

```

```

<400> 37
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60
gcgcagtgtt cgctgaagg gttgtagtac cagcgcgagg tgctctcctt gcagagtcct 120
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg 180
tcnaanccac tcgtgtattt ttacangca gcctcctccg aagcncctcg gcagtggggg 240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300
gggctgacag gtgccagaac aactggatn ggcctttcca tggaaaggcc tgggggaaat 360
cncctnancc caaactgcct ctcaaaggcc accttgaca ccccgacag ctagaaatgc 420
actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aaccaaanc 480
ttgcaaaatc tgcctcgtgg ggtcatnnn taccanggtt ggggaaanaa acccgcnng 540
ganccnccct gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaaanagca 600
caattgaact gttaaenttg ggcnggttc cncnnggtg gtctgaaact aatcaccgtc 660
actggaaaaa ggtangtgc ttcttgaat tcccaaannt cccctngnt tgggtntttt 720
ctcctctncc ctaaaaatcg tnttcccccc cctangggc 760

```

18

<210> 38
 <211> 724
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(724)
 <223> n = A,T,C or G

<400> 38
 tttttttttt tttttttttt tttttttttt tttttaaaaa cccctccat tgaatgaaaa 60
 cttccnaaat tgtccaaccc cctcnnccaa atnnccattt cggggggggg gttccaaacc 120
 caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180
 aatttaaccc attatnaact taaatncctn gaaaccctg gnttccaaaa atttttaacc 240
 cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300
 ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt 360
 tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt 420
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tcccnttttg gggccatncc 480
 cccnctttcg ggggttggn ntaggttgaa tttttnnang nccccaaaaa ncccccaana 540
 aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttg gaaaggnggg 600
 tttntggggg ccngggantt cnttcccccn ttncncccc ccccccnggt aaanggttat 660
 ngnttttgtt ttttgggcc cttnanggac cttccggatn gaaattaaat ccccggnccg 720
 gccg 724

<210> 39
 <211> 751
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 39
 tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttggttg ctgctgctgt 120
 tttatttatt ttacttgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180
 ggcgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt 240
 cgcaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300
 ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttttaattana 360
 cttgggggtt ccctccccan accaaccnccn ctgacaaaaa gtgccngccc tcaaatnatg 420
 tccccgcnnt cnttgaaca cacngengaa ngttctcatt ntccccncnc caggtnaaaa 480
 tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn 540
 ccctcaanen aattnctnng ccccggtcnc gentnngtcc cccccgggct ccgggaantn 600
 cccccnga annnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660
 cnnagactnt cctcnnnan cncaattttc ttttnntcac gaacncgnnc cnnaaatgn 720
 nnnncnctc cntnngtcen naatcnccan c 751

<210> 40
 <211> 753
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(753)

<223> n = A, T, C or G

<400> 40

```

gtgggtatttt ctgtaagatc aggtgttcct ccctcgtagg tttagaggaa acaccctcat    60
agatgaaaac cccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg    120
cgccctatgc acagctgggc ccttgagaca gcagggttc gatgtcaggc tcgatgtcaa    180
tggctctggaa gggcgcgctg tacctgcgta ggggcacacc gtcaggggccc accaggaact    240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccagggtgatn agcttggggg    300
cggtcataan cgcggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna    360
ataaaagggtg cgcccccgca ccgttcantc cgcacttctc naanaccatg angttgggct    420
cnaaccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc    480
ttctnctgat gccctanctg gttgcccn gn gccaanca nccccaancc ccggggtcct    540
aaanccaccn cctctcntt tcatctgggt tnttntcccc ggaccttggg tcctctcaag    600
ggancccata tctcnaccan tactcacnt nccccccnt gnnaccanc cttctanngn    660
ttccncccg ncctctggcc cntcaaan gcttnacna cctgggtctg ccttcccccc    720
tnccctatct gnaccnncn tttgtctcan tnt                                     753

```

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

```

actatatcca tcacaacaga catgtttcat cccatagact tcttgacata gtttcaaagt    60
agtgaacca tccttgattt atatacatat atgttctcag tattttggga gcctttccac    120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt    180
tatagcttgt ttacgtagta agtttttgaa gtctacatc aatccagaca cttagttagg    240
tggtaaaactg tgatttttaa aaaatatcat ttgagaatat tcttcagag gtattttcat    300
ttttactttt tgattaattg tgttttatat attagggtag t                                     341

```

<210> 42

<211> 101

<212> DNA

<213> Homo sapien

<400> 42

```

acttactgaa tttagtcttg tgctcttctt tatttagtgt tgtatcataa atactttgat    60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a                                     101

```

<210> 43

<211> 305

<212> DNA

<213> Homo sapien

<400> 43

```

acatctttgt tacagtctaa gatgtgttct taaatcacca ttcttctctg gtcctcacc    60
tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat    120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaacca    180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat    240
tggtatacaga acgagagtta tcttgataa ctcagagctg agtacctgcc cgggggcccgc    300
tcgaa                                     305

```

<210> 44

<211> 852

<212> DNA

<213> Homo sapien

<220>

20

<221> misc_feature
 <222> (1)...(852)
 <223> n = A,T,C or G

<400> 44

acataaatat	cagagaaaag	tagtctttga	aatatattacg	tccaggagtt	ctttgtttct	60
gattatttgg	tgtgtgtttt	ggtttgtgtc	caaagtattg	gcagcttcag	ttttcatttt	120
ctctccatcc	tcgggcattc	ttcccaaatt	tataaccag	tcttcgtcca	tccacacgct	180
ccagaatttc	tctttttag	taatatctca	tagctcggct	gagcttttca	taggtcatgc	240
tgctgtgtt	cttcttttta	ccccatagct	gagccactgc	ctctgatttc	aagaacctga	300
agacgcctc	agatcggtct	tcccatttta	ttaatcctgg	gttcttgtct	gggttcaaga	360
ggatgtcgcg	gatgaattcc	cataagtga	tccctctcgg	gttgtgcttt	ttggtgtggc	420
acttggcagg	gggttcttgc	tcctttttca	tatcagggtga	ctctgcaaca	ggaaggtgac	480
tggtggttgt	catggagatc	tgagcccggc	agaaagtttt	gctgtccaac	aaatctactg	540
tgctaccata	gttgggtgtca	tataaatagt	tctngtcttt	ccagggtgttc	atgatggaag	600
gctcagtttg	ttcagtcctg	acaatgacat	tgtgtgtgga	ctggaacagg	tcactactgc	660
actggccgtt	ccacttcaga	tgctgcaagt	tgctgtagag	gagntgccc	gccgtccctg	720
ccgccgggt	gaactcctgc	aaactcatgc	tgcaaagggtg	ctcgccgttg	atgtcgaact	780
cntggaaagg	gatacaattg	gcatccagct	ggttgggtgc	caggagggtga	tggagccact	840
cccacacctg	gt					852

<210> 45
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 45

acaacagacc	cttgctcgct	aacgacctca	tgctcatcaa	gttggacgaa	tccgtgtccg	60
agtctgacac	catccggagc	atcagcattg	cttcgcagtg	ccctaccgcg	gggaactctt	120
gcctcgtttc	tggttggggg	ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	180
tgaacgtgtc	ggtggtgtct	gaggaggtct	gcagtaagct	ctatgaccgg	ctgt	234

<210> 46
 <211> 590
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(590)
 <223> n = A,T,C or G

<400> 46

actttttatt	taaatgttta	taaggcagat	ctatgagaat	gatagaaaac	atggtgtgta	60
atttgatagc	aatatttttg	agattacaga	gttttagtaa	ttaccaatta	cacagttaaa	120
aagaagataa	tatatccaa	gcanatacaa	aatatcta	gaaagatcaa	ggcaggaaaa	180
tgantataac	taattgacaa	tggaatatca	attttaatgt	gaattgcaca	ttatccttta	240
aaagctttca	aaanaanaa	ttattgcagt	ctanttaatt	caaacagtgt	taaatggtat	300
caggataaan	aactgaagg	canaaaaga	taattttcac	ttcatgtaac	ncaccanatt	360
ttacaatggc	ttaaatgcan	ggaaaaagca	gtggaagtag	ggaagtantc	aaggtctttc	420
tggtctctaa	tctgccttac	tctttgggtg	tggctttgat	cctctggaga	cagctgccag	480
ggctcctgtt	atatccacaa	tcccagcagc	aagatgaagg	gatgaaaaag	gacacatgct	540
gccttccttt	gaggagactt	catctcactg	gccaaactc	agtcacatgt		590

<210> 47
 <211> 774
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(774)
 <223> n = A,T,C or G

<400> 47
 acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60
 tgaacagaat tttcctgnac aacggggcctt caaaataatt ttcttgggga ggttcaagac 120
 gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180
 cattacagac gggactcttg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa 240
 aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggtctt 300
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg 360
 ctggctctg gtcttcagcc cccagctctg gaagcccacc ctctgtgat cctgctggc 420
 ccacactcct tgaacacaca tccccagggtt atattccttg acatggctga acctcctatt 480
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540
 acggcatggg aagcctttct gacttgcctg attactccag catcttggaa caatccctga 600
 ttcccactc cttagaggca agatagggtg gttaagagta gggctggacc acttgagac 660
 aggtgtctg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct 720
 tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt 774

<210> 48
 <211> 124
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(124)
 <223> n = A,T,C or G

<400> 48
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120
 tggt 124

<210> 49
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 49
 gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60
 tgtggctaca ggtgtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120
 ttagggcacc catatcccaa gcantgt 147

<210> 50
 <211> 107
 <212> DNA
 <213> Homo sapien

<400> 50
 acattaaatt aataaaagga ctgttgggggt tctgctaaaa cacatggctt gatatatattgc 60

atggtttgag gttaggagga gttaggcata tgttttgga gaggggt 107

<210> 51
 <211> 204
 <212> DNA
 <213> Homo sapien

<400> 51
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgacgg 60
 cggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgcc cacttgcca 180
 cctccctttt gggaccagca atgt 204

<210> 52
 <211> 491
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(491)
 <223> n = A,T,C or G

<400> 52
 acaaagataa cttttatctt ataacaaaaa tttgatagtt ttaaagggtta gtattgtgta 60
 gggatatttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120
 ccatcagaca ggttttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180
 aaaacttctt gtatcaattt cttttgttca aaatgactga ctttaantatt tttaaatatt 240
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtnc ctcagtcca 300
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360
 atgcaacagt gtcttttctt tntcttttct tttttttttt ttacaggcac agaaactcat 420
 caattttatt tggataacaa aggggtctcca aatttatattg aaaaataaat ccaagttaat 480
 atcactcttg t 491

<210> 53
 <211> 484
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(484)
 <223> n = A,T,C or G

<400> 53
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60
 gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac 120
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180
 caatcaaatc tctacataac actatagtaa ttaaacggtt aaaaaaaagt gttgaaatct 240
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300
 agcttttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct 360
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg 420
 tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480
 cant 484

<210> 54
 <211> 151
 <212> DNA

<213> Homo sapien

<400> 54

```
actaacctc gtgcttgga actccatata gaaaacggg ccatccctga acacggctgg 60
ccactgggta tactgctgac aaccgcaaca acaaaaaca aaatccttgg cactggctag 120
tctatgtcct ctcaagtgcc tttttgttg t 151
```

<210> 55

<211> 91

<212> DNA

<213> Homo sapien

<400> 55

```
acctggcttg tctccgggtg gttcccggtg cccccacgg tccccagaac ggacactttc 60
gccctccagt ggatactcga gccaaagtgg t 91
```

<210> 56

<211> 133

<212> DNA

<213> Homo sapien

<400> 56

```
ggcggatgtg cggttggtat atacaaatat gtcattttat gtaagggtact tgagtatact 60
tggatttttg gtatctgtgg gttgggggga cgggtccagga accaataccc catggatacc 120
aagggacaac tgt 133
```

<210> 57

<211> 147

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(147)

<223> n = A,T,C or G

<400> 57

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actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana 120
tctcantggg ctggatncat gcagggt 147
```

<210> 58

<211> 198

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(198)

<223> n = A,T,C or G

<400> 58

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acagggatat aggtttnaag ttattgtinat tgtaaaatac attgaatttt ctgtatactc 60
tgattacata catttatcct ttaaaaaaga tgtaaatcct aatttttatg ccatctatta 120
atttaccat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180
ttgacttcta agtttggt 198
```

<210> 59

<211> 330
 <212> DNA
 <213> Homo sapien

<400> 59
 acaacaaatg gggtgtgagg aagtcttatac agcaaaactg gtgatggcta ctgaaaagat 60
 ccattgaaaa ttatcattaa tgatttttaa tgacaagtta tcaaaaactc actcaatttt 120
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180
 tacagtcaat aaatgacaaa gccagggcct acaggtgggt tccagacttt ccagaccag 240
 cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt 300
 tttcgtcttt attggacttc tttgaagagt 330

<210> 60
 <211> 175
 <212> DNA
 <213> Homo sapien

<400> 60
 accgtgggtg ccttctacat tcctgacggc tccttcacca acatctgggt ctacttcggc 60
 gtcgtgggtc ccttcctctt catcctcatc cagctgggtc tgctcatcga ctttgccgac 120
 tcctggaacc agcgtgggtc gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61
 <211> 154
 <212> DNA
 <213> Homo sapien

<400> 61
 accccacttt tcctcctgtg agcagtcctg acttctcaact gctacatgat gagggtgagt 60
 ggttggtgct cttcaacagt atcctccctt ttccggatct gctgagccgg acagcagtgc 120
 tggactgcac agccccgggg ctccacattg ctgt 154

<210> 62
 <211> 30
 <212> DNA
 <213> Homo sapien

<400> 62
 cgctcgagcc ctatagttag tcgtattaga 30

<210> 63
 <211> 89
 <212> DNA
 <213> Homo sapien

<400> 63
 acaagtcatt tcagcacctt ttgctcttca aaactgacca tcttttataat ttaatgcttc 60
 ctgtatgaat aaaaatgggt atgtcaagt 89

<210> 64
 <211> 97
 <212> DNA
 <213> Homo sapien

<400> 64
 accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60
 aatcagtgca tccaggattg gtccttggat ctgggggt 97

25

<210> 65
 <211> 377
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(377)
 <223> n = A,T,C or G

<400> 65
 acaacaanaa ntcccttctt taggcactg atggaaacct ggaaccccct tttgatggca 60
 gcatggcgct ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120
 ccaaccctgg tctaccacaca nttctggcta tgggctgtct ctgccactga acatcagggg 180
 tcggtcataa natgaaatoc caanggggac agaggtcagt agaggaagct caatgagaaa 240
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg 300
 tgggggtgaa ctaccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360
 gggcgggagg agcatgt 377

<210> 66
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 66
 acgcctttcc ctcagaattc aggaagaga ctgtcgctg ccttctccg ttgttgcgtg 60
 agaaccctg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120
 aggaactaac tgcaccctgg tcctctcccc agtccccagt tcacctcca tcctcacct 180
 tcctccactc taagggatat caacactgcc cagcacagg gccctgaatt tatgtggttt 240
 ttatatattt ttttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300
 tgttt 305

<210> 67
 <211> 385
 <212> DNA
 <213> Homo sapien

<400> 67
 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga 60
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120
 cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180
 tgtgctgtgc tggagattca cttttgagag agttctctc tgagacctga tctttagagg 240
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300
 cctctcccag ggcccagcc tggccacacc tgcttacagg gcactctcag atgccatac 360
 catagtttct gtgctagtgg accgt 385

<210> 68
 <211> 73
 <212> DNA
 <213> Homo sapien

<400> 68
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60
 gtttttttaa tgg 73

<210> 69
 <211> 536
 <212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttgggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccgggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtccct	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccctta	acaggggccc	tctcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tcctcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagtgt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	táccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatacagg	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtttg	aaaaagaaaa	tctccagcaa	gcatctcatt	240
taaataaagg	tttgtcatct	ttaaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaatagggtg	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	cccttgaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacaac	agtatataag	gctgtaaaat	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(511)
 <223> n = A,T,C or G

<400> 72
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta 60
 aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180
 aaacatggan agattggtgc tgganacgc cgtggctatt cctcattgtt attacanagt 240
 gaggttctct gtgtgccac tggtttgaac accgttctnc aataatgata gaatagtaca 300
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420
 atttctctcc attgcagcna naaaccggtt cttctaagca aacncagggtg atgatggcna 480
 aaatacaccc cctcttgaag naccnggagg a 511

<210> 73
 <211> 499
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(499)
 <223> n = A,T,C or G

<400> 73
 cagtgccagc actgggtgcca gtaccagtag caataacagt gccagtgccca gtgccagcac 60
 cagtgggtgc ttccagtgtg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120
 tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180
 caagtggagat tttagatatt gttaatcctg ccagtccttc tcttcaagcc aggggtgcac 240
 ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca 300
 ctctgcattha aatctatttg ccatttctga aaaaaaaaaa aaaaaaaggc cggccgctcg 360
 antctagagg gcccggttaa acccgctgat cagcctcgac tgtgccttct anttgccagc 420
 catctgttgt ttgccctcc cccgntgcct tccttgaccc tggaaagtgc cactccact 480
 gtcctttcct aantaaat 499

<210> 74
 <211> 537
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(537)
 <223> n = A,T,C or G

<400> 74
 tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat 60
 ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact 120
 tccaggccca cggtcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180
 cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga 240
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300
 ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc 360
 cagtttgctt gatataattg ttgatattaa gattcctgac ttatatattg aatgggttct 420
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480
 tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccg 537

<210> 75
 <211> 467
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(467)
 <223> n = A,T,C or G

<400> 75
 caaanacaat tgttcaaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60
 tgcataattac acgtacctcc tctgtctcct caagtagtgt ggtctatattt gccatcatca 120
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
 tggcacaagg aggccatctt ttccctcatcg gttattgtcc ctagaagcgt cttctgagga 240
 tctagtggg ctttctttct gggtttgggc catttcantt ctcattgtgtg tactattcta 300
 tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76
 <211> 400
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(400)
 <223> n = A,T,C or G

<400> 76
 aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgcgtac 60
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120
 atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat 180
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag 240
 acttgtcttt cagcaaggac tgggtctttct atctcttgta ctacactgaa ttcaccccca 300
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360
 ttnagtggga tcganacatg taagcagcan catggggaggt 400

<210> 77
 <211> 248
 <212> DNA
 <213> Homo sapien

<400> 77
 ctggagtgcc ttgggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
 ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgctgc 120
 caggcactgt tcatctcagc ttttctgtcc ctttgctccc ggcaagcgct tctgctgaaa 180
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240
 aaaaaaaa 248

<210> 78
 <211> 201
 <212> DNA
 <213> Homo sapien

<400> 78

```

actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca    60
tcacccagac ccgcccctgc cegtgcacca cgctgctgct aacgacagta tgatgcttac    120
tctgtacttc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataatgcct    180
gatttaaaaa aaaaaaaaaa a                                201

```

```

<210> 79
<211> 552
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(552)
<223> n = A,T,C or G

```

```

<400> 79
tccttttggt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg    60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt    120
cctctttcct ctgaagatta atgaagttag aaattgaggt ggataaatac aaaaaggtag    180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt    240
atgcaagtta gtaattactc aggtttaact aaattacttt aatatgctgt tgaacctact    300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga    360
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tgggaatttta    420
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac    480
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa    540
aaaaaaaaaa aa                                552

```

```

<210> 80
<211> 476
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga    60
ggggaaaaatg gggccctagaa gttacagagc atctagctgg tgcgctggca cccctggcct    120
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt    180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta    240
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac    300
tcttctaagt cctcttcacg cctcactttg agtcctcctt gggggttgat aggaantntc    360
tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat    420
gctgaaaaaa ttaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa    476

```

```

<210> 81
<211> 232
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

```

```

<400> 81

```

```

tttttttttg tatgcentcn ctgtggngtt attgttgctg ccacctgga ggagcccagt      60
ttcttctgta tctttctttt ctgggggatc ttcttggtc tgccctcca ttcccagcct      120
ctcatcccca tcttgcactt ttgctagggg tggaggcgct ttcttggtag cccctcagag      180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct              232

```

```

<210> 82
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

```

```

<400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc      60
agtaccagta ccaataacat gccagtgccg gtgccagcac cagtgggtggc ttcagtgtctg      120
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctggtg      180
ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt      240
gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac      300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg      360
ccatttcaaa aaaaaaaaaa aaa              383

```

```

<210> 83
<211> 494
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

```

```

<400> 83
accgaattgg gaccgctggc ttataagcga tcatgtcttc cagtattacc tcaacgagca      60
gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc      120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa      180
acgcttcaag gtgctcatga cccagcaacc ggcacctgtc ctctgagggg ccttaaactg      240
atgtcttttc tgccacctgt taccctcggg agactccgta accaaactct tcggactgtg      300
agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat      360
tatgcttgtg tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt      420
tttcncatat tttaaattac naccagaata ntccagaata aatgaattga aaaactctta      480
aaaaaaaaaa aaaa              494

```

```

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca      60
agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag      120

```

```

gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgcaa ctggctggtg 240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg 300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
agcgttnccg cctcatccgg 380

```

```

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

```

```

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
tnccatcgct atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgtctcg tcttccccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagttag gtcaccagcc 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtaggnng gcntnccttt 480
t 481

```

```

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
acttgaaaaa gcaacttnaa gcctggacac tggattataa attcacaata tgcaacactt 120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

```

```

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

```

<400> 87

```



```

agaaccagt atctctnaaa acaacctctc ataccttggt gacctaatTT tgtgtgcgtg      60
tgtgtgtgcg cgcataattat atagacaggc acatctTTTT tacttttgta aaagcttatg      120
cctcttttgg atctatatct gtgaaagtTT taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaagtgt actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa ttccagatn acaacactna caaactctcc cttgactagg      300
ggggacaaaag aaaagcanaa ctgaacatna gaaacaattn cctgggtgaga aattncataa      360
acagaaattg ggtngtatat tgaaanannng catcattnaa acgtTTTTTT ttt          413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgccgt ccccaactccc cgcgtcccgc      60
gtcctagcnn accatggcgg gggccctgcg cgccccgctg ctccgtgctgg ccacctctggc      120
cgtggccctg gccgtgagcc ccgcggcccg ctccagtccc ggcaagccgc cgcgcctggt      180
gggaggccca tggaccocgc gtggaagaag aaggtgtgcg gcgtgcactg gactttgccg      240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc      300
cccaancaaa ttgttactng gggtaantaa ttcttgaag ttgaacctgg gccaaacnng      360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg      420
gaancantcc tgntcttttc caaatTTT          448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca      60
gtagtgatTC tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc      120
agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt      180
ctcagtgaca agttntttct gatgcgaagt tctnattcca gtgttttagt cctttgcacC      240
tttnatgtnn agacttgcct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg      300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn      360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn      420
aattcnmana anttcagtnn tcatacaaca naacngganc ccc          463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

```

```

<400> 90
agggattgaa ggtctnttnt actgtcggac tgttcaccca ccaactctac aagtgtgtgt      60
cttcactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaagt      120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact      180
tcctttgtta agacttcac tcgttaaagtc ttaagttttg tagaaaggaa ttttaattgct      240
cgttctctaa caatgtcctc tccttgaagt atttggtga acaaccacc tnaagtcct      300
ttgtgcatoc attttaata tacttaatat ggcattggtn cactagggtta aattctgcaa      360
gagtcactctg tctgcaaaag ttgcgttagt atatctgcc      400

```

```

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

```

```

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcctcttt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nncgctctt      180
tgtggaaaaa ctggcacttg nctggaaacta gcaagacatc acttacaagt tcacccacga      240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt      300
tgtcaatact aaccgctggg ttgtcctcca tcacatttgt gatctgtagc tctggataca      360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctggt      420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa      480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

```

```

<400> 92
atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact      60
ggtcccgtg tagcccagc gactctccac ctgttggaag cggttgatgc tgcactcctt      120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt      180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc      240
tgcagcgaag ctctctgatg gtcattgagc ggaagcgaat gangcccagg gccttgccca      300
gaaccttccg cctgttctct ggcgctacct gcagctgctg ccgctnacac tcggcctcgg      360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgctcc      420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg      477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

```

```

<400> 93
gaacggctgg accttgctc gcattgtgct gctggcagga ataccttggc aagcagctcc 60
agtccgagca gccccagacc gctgcccgc gaagctaagc ctgcctctgg ccttcccctc 120
cgctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn 180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa 240
caacaacaaa ataacatggt tgccgtttna gttgtataaa agtangtgat tctgtatnta 300
aagaaaatat tactgttaca tatactgctt gcaantttctg tattttattgg tncctctggaa 360
ataaatatat tattaata 377

```

```

<210> .94
<211> 495
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg ggtaggggtc cagttcccag tggagaagaa aggccaggag aantgcgtgc 60
cgagctgang cagatttccc acagtgacct cagagccctg ggctatagtc tctgaccctc 120
ccaaggaaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg 180
gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgcccccc 240
acgaggaana ggccctgant cctgggatca nacacccctt cactgtatc cccacacaaa 300
tgcaagctca ccaaggtccc ctctcagtc ctccctaca ccctgaacgg ncaactggccc 360
acacccaccc agancancca cccgccatgg ggaatgtncct caaggaatcg cngggcaacg 420
tggactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana 480
aaaaaaaaana aaaaaa 495

```

```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt 120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact 180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt 240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta 300
atcggaacaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac 360
ttggttattt tattgtaaat gaattacaaa attcctaatt taagaaaatg gtangttata 420
tttanttcan taatttcttt ccttgtttac gtttaattttg aaaagaatgc at 472

```

```

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

```

35

<222> (1)...(476)

<223> n = A,T,C or G

<400> 96

ctgaagcatt	tcttcaaact	tntctacttt	tgtcattgat	acctgtagta	agttgacaat	60
gtgggtgaaat	ttcaaaaatta	tatgtaactt	ctactagttt	tactttctcc	cccaagtctt	120
ttttaactca	tgattttttac	acacacaatc	cagaacttat	tatatagcct	ctaagtcttt	180
attcttcaca	gtagatgatg	aaagagtcc	ccagtgtctt	gngcanaatg	ttctagntat	240
agctggatac	atacngtggg	agttctataa	actcatacct	cagtgggact	naaccaaaat	300
tgtgttagtc	tcaattcccta	ccacactgag	ggagcctccc	aaatcactat	attcttatct	360
gcaggtactc	ctccagaaaa	acngacaggg	caggcttgca	tgaaaaagtn	acatctgcgt	420
tacaaagtct	atcttcctca	nangtctgtn	aaggaacaat	ttaatcttct	agcttt	476

<210> 97

<211> 479

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(479)

<223> n = A,T,C or G

<400> 97

actcttttcta	atgctgatat	gatcttgagt	ataagaatgc	atatgtcact	agaatggata	60
aaataatgct	gcaaacttaa	tgttcttatg	caaaatggaa	cgctaataa	acacagctta	120
caatcgcaaa	tcaaaactca	caagtgtctca	tctgttttag	atttagtgta	ataagactta	180
gattgtgctc	cttcggatat	gattgtttct	canatcttgg	gcaatnttcc	ttagtcaaat	240
caggctacta	gaattctgtt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcaact	tatacctgct	atcagcagct	agaaaaacat	360
ntnnntttta	natcaaagta	ttttgtgttt	ggaantgttn	aaatgaaatc	tgaatgtggg	420
ttcnatctta	ttttttcccn	gacnactant	tnctttttta	gggnetatc	tganccatc	479

<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtctc	tgctacttat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttcctctac	ggatgagaga	ctggctcaag	aatacctca	tgcagcttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaaa	300
ttacctggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
tttaagaaaa	ctaccacatg	ttgtgtatcc	tggtgcccgc	cgtttatgaa	ctgaccaccc	420
tttgaataaa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

<210> 99

<211> 171

<212> DNA

<213> Homo sapien

<400> 99

gtggccgcgc	gcaggtgttt	cctcgtagcg	cagggccccc	tccttccccc	aggcgtccct	60
cggcgccctc	gcgggcccga	ggaggagcgg	ctggcggtg	gggggagtgt	gaccacccct	120
cggtgagaaa	agccttctct	agcgatctga	gaggcgtgcc	ttgggggtac	c	171

36

<210> 100
 <211> 269
 <212> DNA
 <213> Homo sapien

<400> 100
 cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc 60
 cgactgcgac gacggcgccg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120
 aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180
 cagccggaac agagcccggg gaagcgggag gcctcgggga gcccctcggg aaggcgggcc 240
 cgagagatac gcaggtgcag gtggccgcc 269

<210> 101
 <211> 405
 <212> DNA
 <213> Homo sapien

<400> 101
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 gctagcaagg taacagggtg gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg 120
 ttgattggtt tgtctttatg gggcggggtt ggggtagggg aaacgaagca aataacatgg 180
 agtgggtgca ccctccctgt agaacctggt tacaagctt ggggcagttc acctggtctg 240
 tgaccgtcat tttcttgaca tcaatgttat tagaagtcag gatattcttt agagagtcca 300
 ctgttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagttg 360
 gatgatcagt acgaataccg aggcataatc tcatatcggt ggcca 405

<210> 102
 <211> 470
 <212> DNA
 <213> Homo sapien

<400> 102
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 ggcacttaac ccatttttat ttcaaaatgt ctacaaattt aatccatta tacggtattt 120
 tcaaaatcta aattattcaa attagccaaa tccttaccaa ataataccca aaaatcaaaa 180
 atatacttct tttagcaaac ttgttacata aattaaaaaa atatatacgg ctggtgtttt 240
 caaagtacaa ttatcttaac actgcaaaaca ttttaaggaa ctaaaataaa aaaaaacact 300
 ccgcaaagggt taaagggaac aacaaattct tttacaacac cattataaaa atcatatctc 360
 aaatcttagg ggaatatata ctacacacgg gatcttaact tttactcact ttgtttattt 420
 ttttaaacca ttgtttgggc ccaacacaat ggaatcccc ctggactagt 470

<210> 103
 <211> 581
 <212> DNA
 <213> Homo sapien

<400> 103
 tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttattttact 60
 tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac 120
 taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt 180
 gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240
 atttttcttg tctttaaaaa tatctaattc ttccattttt tccctattcc aagtcaattt 300
 gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360
 agggaaaaaca ggaagagaaa tggcacacaa aacaaacatt ttatattcat atttctacct 420
 acgttaataa aatagcattt tgtgaagcca gctcaaaaga aggccttagat ccttttatgt 480
 ccatttttag cactaaacga tatcaaaagt ccagaatgca aaagggttgt gaacatttat 540
 tcaaaagcta atataagata tttcacatac tcatctttct g 581

37

<210> 104
 <211> 578
 <212> DNA
 <213> Homo sapien

<400> 104
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 ctcttatgct atatcatatt ttaagttaaa ctaatgagtc actggcttat cttctcctga 180
 aggaaatctg ttcattcttc tcattcataat agttatatca agtactacct tgcataattga 240
 gaggtttttt ttctctatct acacatatat ttccatgtga atttgtatca aacctttatt 300
 ttcatgcaaa ctgaaaaata atgtttcttt tgcataagag aagagaacaa tatagcatta 360
 caaaactgct caaattgttt gttaagttat ccattataat tagttggcag gagctaatac 420
 aaatcacatt tacgacagca ataataaaac tgaagtacca gttaaatatc caaaataatt 480
 aaaggaacat ttttagcctg ggtataatta gctaattcac tttacaagca tttattagaa 540
 tgaattcaca tgttattatt cctagcccaa cacaatgg 578

<210> 105
 <211> 538
 <212> DNA
 <213> Homo sapien

<400> 105
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 gtcttgaaca ccaatattaa ttgaggaaa atacaccaaa atacattaag taaattattt 180
 aagatcatag agcttgtaag tgaagagata aaatttgacc tcagaaaactc tgagcattaa 240
 aaatccacta ttagcaaata aattactatg gacttcttgc ttttaatttt tgatgaatat 300
 ggggtgtcac tggtaaacca acacattctg aaggatacat tacttagtga tagattctta 360
 tgtactttgc taatacgtgg atatgagttg acaagtttct ctttcttcaa tcttttaagg 420
 ggcgagaaat gaggaagaaa agaaaaggat tacgcatact gttctttcta tggaaggatt 480
 agatatgttt cctttgccaa tattaataaaa ataataatgt ttactactag tgaaaccc 538

<210> 106
 <211> 473
 <212> DNA
 <213> Homo sapien

<400> 106
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 tttataaatg taagtgcca ttattgagta atatattcct ccaagagtgg atgtgtocct 180
 tctcccacca actaatgaac agcaacatta gtttaatttt attagtagat atacactgct 240
 gcaaacgcta attctcttct ccattcccat gtgatattgt gtatatgtgt gagttggtag 300
 aatgcatcac aatctacaat caacagcaag atgaagctag gctgggcttt cggtgaaaat 360
 agactgtgtc tgtctgaatc aaatgatctg acctatcctc ggtggcaaga actcttcgaa 420
 ccgcttctct aaaggcgctg ccacatttgt ggctctttgc acttgtttca aaa 473

<210> 107
 <211> 1621
 <212> DNA
 <213> Homo sapien

<400> 107
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 ccgctacgac gtgagccgct tgggccgggg caagcgctcg ctagtgtctg acctgaagca 180
 gccgcgggga gccgcgctgc tgcggcgtct gtgcaagcgg tcggatgtgc tgctggagcc 240

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cttcgcccgc ggtgtcatgg agaaactcca gctgggcccga gagattctgc agcgggaaaa 300
tccaaggcctt atttatgccca ggctgagtggtg atttggccag tcaggaagct tctgccgggtt 360
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tggtgagaat ccgtatgccc cgctgaatct cctggctgac tttgctggtg gtggccttat 480
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cattgatgca aatatggtgg aaggaacagc atatttaagt tcttttctgt ggaaaactca 600
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atttacactc ttgattctac aatgtagaaa atgaggaaat gccacaaatt gtatggtgat 1560
aaaagtcacg tgaacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
a

```

<210> 108
 <211> 382
 <212> PRT
 <213> Homo sapien

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<400> 108
Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1 5 10 15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20 25 30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35 40 45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50 55 60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65 70 75 80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85 90 95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100 105 110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115 120 125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130 135 140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Leu Met Cys
145 150 155 160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165 170 175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180 185 190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195 200 205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg

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. 39

210	215	220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe		
225	230	235
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro		240
	245	250
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala		255
	260	265
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp		270
	275	280
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val		285
	290	295
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu		300
305	310	315
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala		320
	325	330
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu		335
	340	345
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn		350
	355	360
Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu		365
370	375	380

<210> 109
 <211> 1524
 <212> DNA
 <213> Homo sapien

<400> 109

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cagtgcgacc	tagtggtctt	cacctgcttc	ctcctgggcg	tgggctgccg	gctgaccccg	180
ggttttgtacc	acctggggcg	cactgtcctc	tgcctcgact	tcatggtttt	cacggtgctg	240
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atgatgaagg	acgtgttctt	cttctctctt	ttcctcggcg	tgtggctggt	agcctatggc	360
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cagaggaaaa	aaaaaaaaaa	aaaa				1524

<210> 110
 <211> 3410
 <212> DNA

<213> Homo sapien

<400> 110

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tagcgggggtg	aatattttat	actgtaagt	agcaatcaga	gtataatgtt	tatggtgaca	3300

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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaataa aaaaaaaaaa 3410

<210> 111
 <211> 1289
 <212> DNA
 <213> Homo sapien

<400> 111
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 gtggagcctc agcagttccc tctttcagaa ctcaactgcca agagccctga acaggagcca 120
 ccatgcagtg cttcagcttc attagacca tgatgatcct cttcaatttg ctcacttttc 180
 tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcatcctttc 240
 tgaagatctt cgggccactg tctccagtg ccatgcagtt tgtcaacgtg ggctacttcc 300
 tcatcgcagc cggcgttgtg gtctttgtct ttggtttccct gggctgctat ggtgctaaga 360
 ctgagagcaa gtgtgccctc gtgacgttct tcttcaccc cctcctcatc ttcattgctg 420
 aggttgacgc tgctgtggtc gccttgggtg acaccacaat ggctgagcac ttcctgacgt 480
 tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt 540
 ggaacaccac catgaaaggc ctcaagtgtc gtggcttcac caactatacg gattttgagg 600
 actcacccta cttcaaagag aacagtgcct ttccccatt ctgttgcaat gacaacgtca 660
 ccaacacagc caatgaaacc tgcaccaagc aaaaggctca cgaccaaaaa gtagagggtt 720
 gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag 780
 ctggaattgg gggcctcgag ctggctgcca tgattgtgtc catgtatctg tactgcaatc 840
 tacaataagt ccacttctgc ctctgccact actgctgcca catgggaact gtgaaggagg 900
 accctggcaa gcagcagtg tggggggagg ggacaggatc taacaatgtc acttgggcca 960
 gaatggacct gccctttctg ctccagactt ggggctagat agggaccact ccttttagcg 1020
 atgcctgact ttccttccat tgggtgggtg atgggtgggg ggcatccag agcctctaag 1080
 gtagccagtt ctgttgccca ttccccagct ctattaaacc cttgatatgc cccctaggcc 1140
 tagtggtgat cccagtgtc tactggggga tgagagaaag gcattttata gcctgggcat 1200
 aagtgaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc 1260
 tgttacaatg ttaaaaaaaaa aaaaaaaaaa 1289

<210> 112
 <211> 315
 <212> PRT
 <213> Homo sapien

<400> 112
 Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
 1 5 10 15
 Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
 20 25 30
 Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
 35 40 45
 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
 50 55 60
 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
 65 70 75 80
 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
 85 90 95
 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
 100 105 110
 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
 115 120 125
 Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
 130 135 140
 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
 145 150 155 160

42

Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
 165 170 175
 Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
 180 185 190
 Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu
 195 200 205
 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
 210 215 220
 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
 225 230 235 240
 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
 245 250 255
 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
 260 265 270
 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
 275 280 285
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly
 290 295 300
 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
 305 310 315

<210> 113

<211> 553

<212> PRT

<213> Homo sapien

<400> 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
 1 5 10 15
 Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu
 20 25 30
 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val
 35 40 45
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
 50 55 60
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
 65 70 75 80
 Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
 85 90 95
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
 100 105 110
 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
 115 120 125
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
 130 135 140
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
 145 150 155 160
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
 165 170 175
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
 180 185 190
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
 195 200 205
 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
 210 215 220
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
 225 230 235 240
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu

43

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                245                250                255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg
                260                265                270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
                275                280                285
Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
                290                295                300
Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
305                310                315                320
Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
                325                330                335
Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
                340                345                350
Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
                355                360                365
Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
370                375                380
Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
385                390                395                400
Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
                405                410                415
Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
                420                425                430
Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
                435                440                445
Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser
                450                455                460
Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
465                470                475                480
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
                485                490                495
Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
                500                505                510
Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
                515                520                525
Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
                530                535                540
Lys Ser Asp Leu Ala Lys Tyr Ser Ala
545                550

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<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

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Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
1                5                10                15
Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
                20                25                30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
                35                40                45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
                50                55                60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
65                70                75                80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
                85                90                95

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Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
 130 135 140
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
 145 150 155 160
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
 165 170 175
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
 180 185 190
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
 195 200 205
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
 210 215 220
 Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
 225 230 235 240
 Gln

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400> 115
 gctctttctc tcccctcctc tgaatttaat tctttcaact tgcaatttgc aaggattaca 60
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180
 actggtagaa aaacatctga agagctagtc tatcagcattc tgacagggtga attggatggt 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300
 tctctacatg catacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360
 ttagtc 366

<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400> 116
 acaaagatga accatttcct atattatagc aaaattaaaa tctacccgta ttctaattatt 60
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120
 agactttact attttcatat tttaagacac atgattttatc ctatttttagt aacctggttc 180
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>

45

<221> misc_feature
 <222> (1)...(305)
 <223> n = A,T,C or G

<400> 117
 acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca 60
 tattttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120
 aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga 180
 tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt 240
 gactgccccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat 300
 tgggt 305

<210> 118
 <211> 71
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(71)
 <223> n = A,T,C or G

<400> 118
 accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa 60
 aantcctggg t 71

<210> 119
 <211> 212
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(212)
 <223> n = A,T,C or G

<400> 119
 actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca 60
 gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac 120
 agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant 180
 aatggantca aganactccc aggcctcagc gt 212

<210> 120
 <211> 90
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(90)
 <223> n = A,T,C or G

<400> 120
 actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctettgcc 60
 ctccgccggc gcagaacatg ctgggggtgt 90

<210> 121
 <211> 218

46

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(218)
 <223> n = A,T,C or G

<400> 121
 tgtancgtga anacgacaga nagggttgct aaaaatggag aanccttgaa gtcattttga 60
 gaataagatt tgctaaaaga tttggggcta aaacatgggt attgggagac atttctgaag 120
 atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc 180
 agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122
 <211> 171
 <212> DNA
 <213> Homo sapien

<400> 122
 taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg 60
 catttgtag ctcatggaac aggaagtcgg atgggtggggc atcttcagtg ctgcatgagt 120
 caccaccccg gcggggtcat ctgtgccaca ggtccctggt gacagtgcgg t 171

<210> 123
 <211> 76
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(76)
 <223> n = A,T,C or G

<400> 123
 tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca 60
 ttatcaanta ttgtgt 76

<210> 124
 <211> 131
 <212> DNA
 <213> Homo sapien

<400> 124
 acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60
 caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg 120
 ttaagatttg t 131

<210> 125
 <211> 432
 <212> DNA
 <213> Homo sapien

<400> 125
 actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg 60
 cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa 120
 ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180
 ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240

47

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ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300
catggtgggg gtcttgcata tgtaagaatg gaattgattt tgcttttgca agaattctcag 360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcctctc 420
ctctttgctt gt 432

```

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<210> 126
<211> 112
<212> DNA
<213> Homo sapien

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<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60
agtaagaatg atatttcccc ccagggatca ccaaataatt ataaaaattt gt 112

```

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<210> 127
<211> 54
<212> DNA
<213> Homo sapien

```

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<400> 127
accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

```

```

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

```

```

<400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
ttctctctga agtctagggt acccattttg gggaccatt ataggcaata aacacagttc 180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttctttt tcttagcctt 240
ttcctgcaaa aggctcactc agtcccctgc ttgctcagtg gactgggctc cccagggcct 300
aggctgcctt cttttccatg tcc 323

```

```

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(192)
<223> n = A,T,C or G

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```

<400> 129
acatacatgt gtgtatatat ttaaataatca cttttgtatc actctgactt tttagcatac 60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcacc 120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180
gataaacaaa gt 192

```

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<210> 130
<211> 362
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```


48

<222> (1)...(362)

<223> n = A,T,C or G

<400> 130

ccctttttta	tggaatgagt	agactgtatg	tttgaanatt	tanccacaac	ctctttgaca	60
tataatgacg	caacaaaaag	gtgctgttta	gtcctatggg	tcagtttatg	cccctgacaa	120
gtttccattg	tgttttgccg	atcttctggc	taatcgtggg	atcctccatg	ttattagtaa	180
ttctgtatcc	cattttgtta	acgcctggta	gatgtaacct	gctangaggc	taactttata	240
cttattttaa	agctcttatt	ttgtgggtcat	taaaatggca	atttatgtgc	agcactttat	300
tgcagcagga	agcacgtgtg	ggttgggtgt	aaagctcttt	gctaactcta	aaaagtaatg	360
gg						362

<210> 131

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(332)

<223> n = A,T,C or G

<400> 131

ctttttgaaa	gatcgtgtcc	actcctgtgg	acatcttggt	ttaatggagt	ttcccatgca	60
gtangactgg	tatggttgca	gctgtccaga	taaaaacatt	tgaagagctc	caaaatgaga	120
gttctcccag	gttcgccttg	ctgctccaag	tctcagcagc	agcctctttt	aggaggcatc	180
ttctgaacta	gattaaggca	gcttgtaaat	ctgatgtgat	ttgggtttatt	atccaactaa	240
cttccatctg	ttatcactgg	agaaagccca	gactccccan	gacnggtacg	gattgtgggc	300
atanaaggat	tggttgaagc	tggcgttggt	gt			332

<210> 132

<211> 322

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(322)

<223> n = A,T,C or G

<400> 132

actttttgcca	ttttgtatat	ataaacaatc	ttgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggctaag	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaattcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggt	180
tttagcaagt	taaaatgaan	atgacaggaa	aggcttattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	agggaagcct	300
gtaacaatct	acaattgggtc	ca				322

<210> 133

<211> 278

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(278)

<223> n = A,T,C or G

```

<400> 133
acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt    60
cttggtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta    120
ctattttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg    180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt    240
cccacgaaac actaataaaa accacagaga ccagcctg                                278

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```

<210> 134
<211> 121
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(121)
<223> n = A,T,C or G

```

```

<400> 134
gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca    60
tgattctctg aggttaaact tggttttcaa atgttatatt tacttgattt ttgcttttgg    120
t                                                                    121

```

```

<210> 135
<211> 350
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(350)
<223> n = A,T,C or G

```

```

<400> 135
acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc    60
atancaagtg gtgactgggt aagcgtgcga caaaggtcag ctggcacatt acttggtgtgc    120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tgggtactcca    180
gggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct    240
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag    300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt                350

```

```

<210> 136
<211> 399
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(399)
<223> n = A,T,C or G

```

```

<400> 136
tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt    60
gctgtgattg tatccgaata ntctcgtga gaaaagataa tgagatgacg tgagcagcct    120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga    180
cctggcggcc agccagccag ccacaggtgg gcttcttctt tttgtggtga caacnccaag    240
aaaactgcag aggccagggt tcaggtgtna gtgggtangt gaccataaaa caccaggtgc    300
tcccaggaac cggggcaaag gccatcccca cctacagcca gcatgccac tggcgtgatg    360
ggtgcagang gatgaagcag ccagntgttc tgctgtggt                                399

```

50

<210> 137
 <211> 165
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(165)
 <223> n = A,T,C or G

<400> 137
 actggtgtgg tnggggtga tgctgggtgt anaagttgan gtgacttcan gatggtgtgt 60
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120
 ttggctggtc ccactggtgg tcaactgtcat tgggtggggtt cctgt 165

<210> 138
 <211> 338
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(338)
 <223> n = A,T,C or G

<400> 138
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccac 120
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180
 tcatgtgttt ccagccacac caaaagggtc ttgggggtgga gggctggggg catananggt 240
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139
 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 139
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccga gtgaaggaga 120
 attcaaacag acctcgatc tcttggtgtg agcctgggtg gctcaccgcc tatcatctgc 180
 atttgccctta ctcagggtgct accggactct ggccoctgat gtctgtagtt tcacaggatg 240
 ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300
 gtcagctatg tgccccatcc tccttcacgc cctccctccc tttcctacca ctgctgagtg 360
 gcctggaact tgtttaaagt gt 382

<210> 140
 <211> 200
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(200)
 <223> n = A,T,C or G

```

<400> 140
accaaaancctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat      60
acttttcatt taacancctt tgtaagtgt caggctgcac ttgtctccat anaattattg      120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt      180
atattcagca taaaggagaa                                200

```

```

<210> 141
<211> 335
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(335)
<223> n = A,T,C or G

```

```

<400> 141
actttattttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg      60
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt      120
atgcatgtag agaaccctaaa ctaattttatt aaacaggata gaaacaggct gtctgggtga      180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg      240
tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaa agcaagatgg      300
attcaçaaac caagtaattt taaacaaaga cactt                                335

```

```

<210> 142
<211> 459
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(459)
<223> n = A,T,C or G

```

```

<400> 142
accagggttaa tattgccaca tatatccttt ccaattgagg gctaaacaga cgtgtattta      60
gggttggtta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat      120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca      180
cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc      240
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca      300
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga      360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct      420
cagcangggg gggaggaacc agctcaacct tggcgtant                                459

```

```

<210> 143
<211> 140
<212> DNA
<213> Homo sapien

```

```

<400> 143
acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg      60
aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag      120
accatccgac ttccctgtgt                                140

```

```

<210> 144
<211> 164
<212> DNA
<213> Homo sapien

```

52

<220>
 <221> misc_feature
 <222> (1)...(164)
 <223> n = A,T,C or G

<400> 144
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg 120
 aggcaattaa tccatatttg ttttcaataa ggaaaaaag atgt 164

<210> 145
 <211> 303
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 145
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaatacaa 60
 actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat 120
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300
 caa 303

<210> 146
 <211> 327
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(327)
 <223> n = A,T,C or G

<400> 146
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60
 actggcctgg agtgactcat tgcctctggt ggttgagaga gctcctttgc caacaggcct 120
 ccaagtcagg gctgggattt gtctccttcc cacttcttag caacaatatg ctggccactt 180
 cctgaacagg gagggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc 240
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300
 taggggtgag ctgtgtgact ctatggt 327

<210> 147
 <211> 173
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(173)
 <223> n = A,T,C or G

<400> 147

53

```

acattgtttt tttagataa agcattgana gagctctcct taacgtgaca caatggaagg      60
actggaacac ataccacat ctttgttctg agggataaatt ttctgataaa gtcttgctgt      120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt              173

```

<210> 148

<211> 477

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(477)

<223> n = A,T,C or G

<400> 148

```

acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct      60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact      120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg      180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgtcac      240
nccancccac ctcaccgacc ccatcctctt acacagctac ctccctgtc tctaacccca      300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag      360
caccactggt aagccttctc cagccaacac acacacacac acacnacac acacacatat      420
ccaggcacag gctacctcat cttcacaatc accccttaa ttaccatgct atgggtg          477

```

<210> 149

<211> 207

<212> DNA

<213> Homo sapien

<400> 149

```

acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac      60
taacgtatit tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct      120
gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca      180
tttcaggcag agggaacagc agtgaaa                207

```

<210> 150

<211> 111

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(111)

<223> n = A,T,C or G

<400> 150

```

accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg      60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t              111

```

<210> 151

<211> 196

<212> DNA

<213> Homo sapien

<400> 151

```

agcgcggcag gtcatttga acattccaga tacctatcat tactcgatgc tgttgataac      60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat      120
ggataccaac cggaaaaccc ctatcccgcg cagcccactg tggccccac tgtctacgag      180

```

54

```

gtgcatccgg ctcagt                                     196

    <210> 152
    <211> 132
    <212> DNA
    <213> Homo sapien

    <400> 152
acagcacttt cacatgtaag aaggagaaa ttcctaaatg taggagaaag ataacagaac      60
cttccccctt tcctctagt gtggaaacct gatgctttat gttgacagga atagaaccag    120
gagggagttt gt                                     132

    <210> 153
    <211> 285
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(285)
    <223> n = A,T,C or G .

    <400> 153
acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag      60
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga    120
gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaaacac    180
cctggctagt gaggtgctgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca    240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt                      285

    <210> 154
    <211> 333
    <212> DNA
    <213> Homo sapien

    <400> 154
accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc      60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac    120
cctaagccgg ttacacagct aactcccaact ggccttgatt tgtgaaattg ctgctgcctg    180
attggcacag gagtccaagg tggttcagtc ccctcctccg tggaacgaga ctctgatttg    240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg    300
gtcaggcctg tctcatccat atggatcttc cgg                                    333

    <210> 155
    <211> 308
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(308)
    <223> n = A,T,C or G

    <400> 155
actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg      60
gaaagtgcct tgggaactgt aaagtgccta acacatgac gatgattttt gttataatat    120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc    180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggct    240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcatgctg    300

```

```

gccctggt 308

    <210> 156
    <211> 295
    <212> DNA
    <213> Homo sapien

    <400> 156
accttgctcg gtgcttgga catattagga actcaaaata tgagatgata acagtgccta 60
ttattgatta ctgagagaac tgtagacat ttagttgaag attttctaca caggaactga 120
gaataggaga ttatgttttg ccctcatatt ctctcctatc ctccctgcct cattctatgt 180
ctaataatatt ctcaatcaaa taaggtttagc ataatcagga aatcgaccaa ataccaatat 240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295

    <210> 157
    <211> 126
    <212> DNA
    <213> Homo sapien

    <400> 157
acaagttaa atagtgtgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct 60
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc 120
cttagt 126

    <210> 158
    <211> 442
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(442)
    <223> n = A,T,C or G

    <400> 158
accactggt cttggaaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg 60
aanccagcag gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt 120
gcctgggtaa ttcaccatta atttctctcc ccaaactctc tgagtcttcc cttaatattt 180
ctggtgggtc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta 240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg 300
ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga 360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg 420
tgttcattct ctgatgtcct gt 442

    <210> 159
    <211> 498
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(498)
    <223> n = A,T,C or G

    <400> 159
acttccaggt aacgttggtg tttccgttga gcctgaactg atgggtgacg ttgtaggttc 60
tccaacaaga actgaggttg cagagcgggt agggaaagat gctgttccag ttgcacctgg 120
gctgctgtgg actgttggtg attcctcact acggcccaag gttgtggaac tggcanaaag 180

```



```

gtgtgttgtt gganttgagc tcgggcggtt gtggtaggtt gtgggctctt caacaggggc 240
tgctgtgggt cggggangtg aangtggtgt gtcacttgag cttggccagc tctggaaagt 300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa 360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn 420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc 480
aagggaataa gctgtggt

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccttg ccaaactcac aaggagacat caacctctag acagggaaac 60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct 120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc 180
cactagacat ctcacagacc acttgtgtga agagatgccc catgacccca gatgcctctc 240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg 300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa 360
cttgtagaat gaagcctgga

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc cctctgagc aggcgggtgt cgttcaaggt gtatttggcc ttgcctgtca 60
cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt 114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa 60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt 120
tggtgatata taacttggca ataaccagct ctggtgatac ataaaactac tcactgt 177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

```

```

<400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac 60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt 120

```

catcagcggc atgatgt

137

<210> 164

<211> 469

<212> DNA

<213> Homo sapien...

<220>

<221> misc_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta	60
tgcaatgcat catgctatct catacctaat gagggagttc caggagattc aaccaggaaa	120
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt	180
gagacatgca cttgtctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg	240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg	300
gtggagaaga aggaccctgt aaagacctgt tctgtcagtg aatggataat ctaatgtgct	360
tctagttagc acagggtctc caggccaggc ctcattctcc tctggcctct aatagtcaat	420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt	469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt atanatatcg acattgccgg cacttggtgtt cagtttcata aagctgggtg	60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc	120
tgcaggccgc ccgccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact	180
tcctctgaga tgagt	195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc	60
cgaggctcga gtccacacca ccggtgtagg tgtgtcctaat cttgggcttg gcgcccacct	120
ttggagaagg gatattgtgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt	180
tttgagacc agcctgagca aggggcggat gttcagcttc agctcctcct tcgtcagggtg	240
gatgcccaacc tcgtctangg tccgtgggaa gctgggtgtcc acntcaccta caacctgggc	300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt	360
nggggccttt ttggtgaact ttc	383

<210> 167

58

<211> 247
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(247)
 <223> n = A,T,C or G

<400> 167
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat 60
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180
 tcaatctgan tccaagtgg tggttggaac actggtcatg acanaggcag tgactctgac 240
 tgangtc 247

<210> 168
 <211> 273
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(273)
 <223> n = A,T,C or G

<400> 168
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60
 aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120
 gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc 180
 aattcccaac ttccttgcca caagcttccc aggttttctc ccctggaaaa ctccagcttg 240
 agtcccagat aactcatgg gctgccttgg gca 273

<210> 169
 <211> 431
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(431)
 <223> n = A,T,C or G

<400> 169
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60
 agctcagacc aggttcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120
 ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag 180
 ggcagcagaa agggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcaactgctg gcaccagctc 300
 acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg 360
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420
 tcgaacactg a 431

<210> 170
 <211> 266
 <212> DNA
 <213> Homo sapien

59

<220>
 <221> misc_feature
 <222> (1)...(266)
 <223> n = A,T,C or G

<400> 170
 acctgtgggc tgggctgtta tgccctgtgcc ggctgtctgaa agggagttca gaggtggagc 60
 tcaaggagct ctgcaggcat ttgtccaanc ctctccanag canagggagc aacctacact 120
 ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat 180
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240
 tcaaagctag gggtctggca ggtgga 266

<210> 171
 <211> 1248
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1248)
 <223> n = A,T,C or G

<400> 171
 ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca 60
 ctggtcatgg aaaacgaatt gttctgtctg ggctcctgg tgcattccga gtgggtgctg 120
 tcagccgcac actgtttcca gaagtgagtg cagagctcct acaccatcgg gctgggcctg 180
 cacagtcttg agcccgacca agagccaggg agccagatgg tggaggccag cctctccgta 240
 cggcacccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac 300
 gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360
 gcggggaaact cttgcctcgt ttctggctgg ggtctgtctg cgaacggcag aatgcctacc 420
 gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac 480
 ccgctgtacc accccagcat gttctgcgcc ggccgagggc aagaccagaa ggactcctgc 540
 aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc 600
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc 660
 actgagtga tagagaaaac cgtccagcc agttaactct ggggactggg aacctatgaa 720
 attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct 780
 ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc 840
 cccagccctc cctccctcag acccaggagt ccagaccccc cagcccctcc tccctcagac 900
 ccaggagtcc agcccctcct ccctcagacc caggagtcca gacccccag cccctcctcc 960
 ctcagaccca ggggtccagg cccccaacc ctcctccctc agactcagag gtccaagccc 1020
 ccaaccntc attccccaga cccagaggtc cagggtccag cccctntcc ctcagaccca 1080
 gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtggc acgttgacct 1140
 aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt 1200
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1248

<210> 172
 <211> 159
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(159)
 <223> Xaa = Any Amino Acid

<400> 172
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1 5 10 15

60

Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
 20 25 30
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
 35 40 45
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
 50 55 60
 Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
 65 70 75 80
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
 85 90 95
 Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
 100 105 110
 Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
 115 120 125
 Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
 130 135 140
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 145 150 155

<210> 173
 <211> 1265
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1265)
 <223> n = A,T,C or G

<400> 173
 ggcagcccgcc actcgagcc ctggcaggcg gcactgggtca tggaaaacga attgttctgc 60
 tcgggcgctcc tgggtgcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc 120
 tacaccatcg ggctgggctt gcacagtctt gaggccgacc aagagccagg gagccagatg 180
 gtggaggcca gcctctccgt acggcaccca gactacaaca gacccttgct cgctaacgac 240
 ctcatgctca tcaagtggga cgaatccgtg tccgagtctg acaccatccg gagcatcagc 300
 attgcttcgc agtgccttac cgcggggaac tcttgctctg tttctggctg gggctctgctg 360
 gcgaacggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg 420
 cgggggctga cccagagctc tgcgtcccg gcagaatgcc taccgtgctg cagtgcgtga 480
 acgtgtcggg ggtgtctgag gaggtctgca gtaagctcta tgaccgctg taccacccca 540
 gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg 600
 ggccctgat ctgcaacggg tacttgagg gccttggtc tttcggaata gccccgtgtg 660
 gccaaagtgg cgtgccagg gtctacacca acctctgcaa attcactgag tggatagaga 720
 aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaataac 780
 atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag 840
 tccaggcccc cagccctcc tcctcaaac caagggtaca gatcccagc ccctcctccc 900
 tcagacccag gagtccagac ccccagccc ctccctcctc agaccagga gtccagcccc 960
 tcctcentca gaccaggag tccagacccc ccagcccctc ctccctcaga cccaggggtt 1020
 gagggcccca acccctcctc ctccagagtc agaggtccaa gcccacaacc cctcgttccc 1080
 cagacccaga ggttnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc 1140
 tagattttcc ctgnacacag tgcccccttg tggngangttg acccaacctt accagttggt 1200
 ttttcatttt tngtcccttt ccctagatc cagaaataaa gtttaagaga ngngcaaaaa 1260
 aaaaa 1265

<210> 174
 <211> 1459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1459)
 <223> n = A,T,C or G

<400> 174
 ggtagccgc acactgtttc cagaagtgcg tgcagagctc ctacaccatc gggctgggccc 60
 tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120
 tacggcacc agagtacaac agacccttgc tgcctaacga cctcatgctc atcaagttgg 180
 acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcctta 240
 ccgcggggaa ctcttgccctc gtttctggct ggggtctgct ggcgaacggt gagctcacgg 300
 gtgtgtgtct gccctcttca aggaggtcct ctgccagtc gcgggggctg acccagagct 360
 ctgctgtcca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga 420
 ngaggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgccggcgg 480
 agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact 540
 caggggaagg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag 600
 atggagagac acacagggag acagtgcaca ctagagagag aaactgagag aaacagagaa 660
 ataaacacac gaataaagag aagcaaaagg agagagaaac agaaacagac atggggaggc 720
 agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgaggggcgt 780
 gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactagaa 840
 atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt 900
 tttatgcatt catgatatac ctttgttgga atttttgat atttctaagc tacacagttc 960
 gtctgtgaat ttttttaaat tgttgcaact ctcctaaaat tttctgatg tgtttattga 1020
 aaaaatccaa gtataagtgg acttgtgcat tcaaacagg gttgttcaag ggtcaactgt 1080
 gtaccagag ggaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa 1140
 aatcaagac tctacaaaga ggctgggag ggtggctcat gcctgtaatc ccagcacttt 1200
 gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260
 gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320
 aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380
 gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440
 caaaaaaaaa aaaaaaaaaa 1459

<210> 175
 <211> 1167
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1167)
 <223> n = A,T,C or G

<400> 175
 ggcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg 60
 gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 180
 ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgtctatc 240
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgag 300
 tgccctaccg cggggaactc ttgcctcgtg tctggctggg gtctgctggc gaacggcaga 360
 atgcctaccg tgctgcaact cgtgaacgtg tcggtgggtg ctgaggangt ctgcagtaag 420
 ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggaggcca agaccagaag 480
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540
 gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc cagggtgtcta caccacctc 600
 tgcaaatcca ctgagtggat agagaaaacc gtccagncca gtttaactctg gggactggga 660
 acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcagggaata tctgttccca 720
 gcccctcctc cctcaggccc aggagtcag gcccccagcc cctcctcctt caaaccagag 780
 gtacagatcc ccagccctc ctccctcaga cccaggagtc cagacccccc agccctcct 840
 ccntcagacc caggagtcca gccctcctc cntcagacgc aggagtcag acccccagc 900

62

```

ccntcntccg tcagaccagc ggggtgcaggc ccccaacccc tcntccntca gagtcagagg      960
tccaagcccc caaccctcgc ttccccagac ccagaggtnc aggtcccagc ccctccctccc      1020
tcagaccagc cgggtccaatg ccacctagan tntccctgta cacagtgcc ccttggtggca      1080
ngttgaccca accttaccag ttgggttttc atttttgtc cctttcccct agatccagaa      1140
ataaagtnta agagaagcgc aaaaaaa                                1167

```

<210> 176

<211> 205

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1) ... (205)

<223> Xaa = Any Amino Acid

<400> 176

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
 50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100          105          110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
115          120          125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
130          135          140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145          150          155          160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
165          170          175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
180          185          190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
195          200          205

```

<210> 177

<211> 1119

<212> DNA

<213> Homo sapien

<400> 177

```

gcgcactcgc agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc      60
gtcctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc      120
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag      180
gccagectct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg      240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct      300
tcgcagtgcc ctaccgcgga gaactcttgc ctctttctg gctggggtct gctggcgaac      360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc      420
caaccctggc agggttgtac catttcggca acttccagtg caaggacgtc ctgctgcac      480

```

63

```

ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgata aactagccag      540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt      600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc      660
cagttatcct cactgaattg agatttcctg cttcagtgct agccattccc acataatttc      720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctgggtactc ccctcacaaa      780
ttcatttctc ctgtttagt gaaagggtgcg ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg      900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgtaaaaaaa aaaaaaaaaa     1119

```

<210> 178
 <211> 164
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(164)
 <223> Xaa = Any Amino Acid

```

<400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
  1             5             10             15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
      20             25             30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
      35             40             45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
      50             55             60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
      65             70             75             80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
      85             90             95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
      100            105            110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
      115            120            125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
      130            135            140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
      145            150            155            160
Pro Gly Thr Leu

```

<210> 179
 <211> 250
 <212> DNA
 <213> Homo sapien

```

<400> 179
ctggagtgcc ttgtgttttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct      120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgtctga      180
aagttcatat ctggagcctg atgtcttaac gaataaagggt cccatgctcc acccgaaaaa      240
aaaaaaaaaa                                     250

```


64

<210> 180
<211> 202
<212> DNA
<213> Homo sapien

<400> 180
actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca 60
tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120
ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc 180
tgatttaaaa aaaaaaaaaa aa 202

<210> 181
<211> 558
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(558)
<223> n = A,T,C or G

<400> 181
tccytttkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60
aatgttttag cagtgttagt aatttcytcg taatgattct gttattactt tcctnattct 120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240
aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300
ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540
caaaaaaaaa aaaaaaaaaa 558

<210> 182
<211> 479
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

<400> 182
acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc 60
agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120
cstcacacag astcccagat agctgggact acaggcacac agtcactgaa gcaggccctg 180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
ctaaggttaa actttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
tactmttcta agtctcttc cagcctcact kkgagtctm cytggggggt gataggaant 360
ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacgcatara 420
awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183
<211> 384
<212> DNA
<213> Homo sapien

65

```

<400> 183
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc      60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgt      120
ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt      180
gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat      240
tgtaatcct gccagtcttt ctcttcaagc cagggtgcat cctcagaaac ctactcaaca      300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt      360
gccatttcaa aaaaaaaaaa aaaa                                     384

```

```

<210> 184
<211> 496
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(496)
<223> n = A,T,C or G

```

```

<400> 184
accgaattgg gaccgtggc ttataagcga tcatgtyynt ccrgtatcac ctcaacgagc      60
agggagatcg agtctatacg ctgaagaaat ttgaccgat gggacaacag acctgctcag      120
cccacctgc tgggtctcc ccagatgaca aatactctsg acaccgaatc accatcaaga      180
aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac      240
tgatgtcttt tctgccacct gttaccctc ggagactccg taaccaaact cttcgactg      300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg      360
attatgcttg tgtgaggcaa tcatggtggc atcaccata aagggaacac atttgacttt      420
tttttctcat attttaaat actacmagaw tattwmagaw waaatgawtt gaaaaactst      480
taaaaaaaaa aaaaaa                                           496

```

```

<210> 185
<211> 384
<212> DNA
<213> Homo sapien

```

```

<400> 185
gctggtagcc tatggcgkgg ccacaggagg ggctcctgag gccacggrac agtgacttcc      60
caagtatcyt gcgcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc      120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct      180
gggcacaccc tccctgggccc caggcgggca cctgcgtctc ccagtatgcc aactggctgg      240
tgggtgctgct cctcgtcatc ttctgctcgc tggccaacat cctgctggtc aacttgctca      300
ttgccatgtt cagttacaca ttcggaagaa tacagggcaa cagcgatctc tactgggaag      360
gcgcagcgtt accgcctcat ccgg                                     384

```

```

<210> 186
<211> 577
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(577)
<223> n = A,T,C or G

```

```

<400> 186
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggctctcgc ttcataccgc      60
tnccatcgtc atactgtagg ttggccacca cytcctggca tcttggggcg gcntaatatt      120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttccgc      180

```

66

```

tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt      240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac      300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaaagt      360
ctcacccaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgccag      420
gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgctw      480
tccttttgac acacaaaaca gttaaaggca ttttcagccc ccagaaantt gtcacatcc      540
aagatntcgc acagcactna tccagttggg attaaat      577

```

<210> 187

<211> 534

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(534)

<223> n = A,T,C or G

<400> 187

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aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw      60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact      120
ttaaacagtg tgtcaatctg ctcccynac tttgtcatca ccagtctggg aakaagggt      180
tgccctattc acacctgtta aaaggcgct aagcattttt gattcaacat ctttttttt      240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc      300
ttcatgggac agagccatyt gatttaaaaa gcaaatgca taatattgag ctttygggagc      360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg      420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg      480
aggatctccc agtttattta ccacttgac aagaaggcgt tttcttcctc aggc      534

```

<210> 188

<211> 761

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(761)

<223> n = A,T,C or G

<400> 188

```

agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatth ttgtgtcggtg      60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tactttttgta aaagcttatg      120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg      300
ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa      360
acagaaatwr gtagtatat tgaarnacag catcattaaa rmgttwtktt wttctocctt      420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa      480
cttgcccttc attacatggt tnaaagtggg gtggtgggcc aaaatattga aatgatggaa      540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac      600
atgcttaatt cagaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta      660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac      720
gaaaataata acattgaaga aaaaanaaaa aaanaaaaaa a      761

```

<210> 189

<211> 482

<212> DNA

<213> Homo sapien

67

<220>
 <221> misc_feature
 <222> (1)...(482)
 <223> n = A,T,C or G

<400> 189
 tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60
 caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120
 aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180
 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240
 tgataggcac aggccacccg gtacagacc ctcggctcct gacaggtnga tttcgaccag 300
 gtcatgtgac cctgcccagg cacagcgta atctggaaaa gacagaatgc tttccttttc 360
 aaatttggt ngtcatngaa ngggcanttt tccaantng gctnggtctt ggtacncttg 420
 gttcggccca gctccncgct caaaaantat tcacccnct ccnaattgct tgcnggnccc 480
 cc 482

<210> 190
 <211> 471
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(471)
 <223> n = A,T,C or G

<400> 190
 tttttttttt ttttaaaaca gtttttcaca aaaaaattta ttagaagaat agtggttttg 60
 aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntctca 120
 aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180
 cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt 240
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300
 tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantnctcta 360
 ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnngt acaaaaaanaa 420
 tctgtaattn anttcaacct ccgtacngaa aaatnttnnt tatacactcc c 471

<210> 191
 <211> 402
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(402)
 <223> n = A,T,C or G

<400> 191
 gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60
 gtcttcact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120
 attcttcacc agtcacatct tctaggacct ttttgattc agttagtata agctcttcca 180
 cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg 240
 ctcgttctct aacaatgtcc tctccttgaa gtatttggtc gaacaaccca cctaaagtcc 300
 ctttgtgcat ccatttttaa tatacttaat agggcattgk tncactaggt taaattctgc 360
 aagagtcac tgtctgcaaa agttgcgtta gtatatctgc ca 402

<210> 192
 <211> 601

68

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(601)
 <223> n = A,T,C or G

<400> 192
 gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnnaact 60
 ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac 120
 atgcytyttt gaytaccgtg tgccaagtgc tgggtgattct yaacacacyt ccatcccggt 180
 cttttgtgga aaaactggca cttktctgga actagcarga catcaacttac aaattcacc 240
 acgagacact tgaaaggtgt aacaaagcga ytcttgcaatt gctttttgtc cctccggcac 300
 cagttgtcaa tactaaccgg ctggtttgcc tccatcacat ttgtgatctg tagctctgga 360
 tacatctcct gacagtactg aagaacttct tcttttggtt caaaagcarg tcttggtgcc 420
 tgttgatca ggttccatt tcccagtcyg aatgttcaca tggcatattt wacttccac 480
 aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag 540
 cctcgatgta gccggccagc gccaaaggcag gcgccgtgag cccaccagc agcagaagca 600
 g 601

<210> 193
 <211> 608
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(608)
 <223> n = A,T,C or G

<400> 193
 atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact 60
 ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt 120
 cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg 180
 tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac 240
 ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc 300
 agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctccggcctc 360
 gaccagcggg caaacggcrt tgaacagccg cacctcacgg atgcccagtg tgtcgcgctc 420
 caggammgsc accagcgtgt ccagggtcaat gtcggtgaag ccctccgagg gtratggcgt 480
 ctgcagtggt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcactgaaga 540
 gtcgcgcctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaaactc 600
 cagcgaat 608

<210> 194
 <211> 392
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(392)
 <223> n = A,T,C or G

<400> 194
 gaacggctgg acctgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt 60
 ccagtcagg cagcccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc 120
 tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg 180

69

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tttgatttta cttggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac 240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt 300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtattttatt gktnctstgg 360
aaataaatat agttattaaa ggttgtcant cc 392

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<210> 195
<211> 502
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

```

```

<400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60
ccgagctgag gcagatgttc ccacagtgc cccagagcc stgggstata gtytctgacc 120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180
aaggggaaggc cccattccgg ggstgttccc cgaggaggaa ggggaaggggc tctgtgtgcc 240
ccccasgagg aagagggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca 300
caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcgggccact 360
gscscacacc caccagagc acgccaccgc ccattggggar tgtgtctcaag gartcgcngg 420
gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480
gctnanaaaa aaaaaaaaaa aa 502

```

```

<210> 196
<211> 665
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(665)
<223> n = A,T,C or G

```

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<400> 196
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkac 240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt 420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt 480
tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540
ttcttagaat gtataaagggt ttagagccat cnaacttcaa agaaaaaat gaccacatac 600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660
aagtg 665

```

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<210> 197
<211> 492
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(492)

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<223> n = A,T,C or G

<400> 197

ttttnttttt	ttttttttgc	aggaaggatt	ccatttattg	tggatgcatt	ttcacaatat	60
atgtttattg	gagcgatcca	ttatcagtga	aaagtatcaa	gtgtttataa	natttttagg	120
aaggcagatt	cacagaacat	gctngtcngc	ttgcagtttt	acctcgtna	gatnacagag	180
aattatagtc	naaccagtaa	acnaggaatt	tacttttcaa	aagattaaat	ccaaactgaa	240
caaaattcta	ccctgaaact	tactccatcc	aaatatggga	ataanagtca	gcagtgtatc	300
attctcttct	gaactttaga	ttttctagaa	aaatatgtaa	tagtgatcag	gaagagctct	360
tgttcaaaag	tacaacnaag	caatgttccc	ttaccatagg	ccttaattca	aactttgatc	420
catttcactc	ccatcacggg	agtcaatgct	acctgggaca	cttgatattt	gttcatnctg	480
ancntggctt	aa					492

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(478)

<223> n = A,T,C or G

<400> 198

tttnttttgn	atttcantct	gtannaanta	ttttcattat	gtttattana	aaaatatnaa	60
tgnttccacn	acaaatcatn	ttacntnagt	aagaggccan	ctacattgta	caacatacac	120
tgagtatatt	ttgaaaagga	caagtttaaa	gtanacncat	attgccganc	atancacatt	180
tatacatggc	ttgattgata	tttagcacag	canaaaactga	gtgagttacc	agaaaanaaat	240
natatatgtc	aatcngattt	aagatacaaa	acagatccta	tggtacatan	catcntgtag	300
gagttgtggc	tttatgttta	ctgaaaagtca	atgcagttcc	tgtacaaaaga	gatggccgta	360
agcattctag	tacctctact	ccatggttaa	gaatcgta	cttatgttta	catatgtnc	420
gggtaagaat	tgtgttaagt	naanttatgg	agaggtccan	gagaaaaatt	tgatncaa	478

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 199

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtctc	tgtcatotat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaacttatt	cctacttgta	cggactttga	180
agtgattcag	tttctctac	ggatgagaga	ctggctcaag	aatatcctca	tcgagcttta	240
tgaagccnac	tctgaacacg	ctggttatct	nagatgagaa	ncagagaaat	aaagtcnaga	300
aaatttacct	ggangaaaag	aggctttngg	ctggggacca	tcccattgaa	ccttctctta	360
anggacttta	agaanaaact	accacatgtn	tgtngtatcc	tggtgccnng	ccgtttantg	420
aacntngacn	ncacccttnt	ggaatanant	cttgacngcn	tcctgaactt	gctcctctgc	480
ga						482

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(270)
 <223> n = A,T,C or G

<400> 200
 cgcccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc 60
 cgactgcgac gacggcgccg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120
 aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180
 cagccggaac agagcccggg gaangcggga ggcctcggg agcccctcgg gaaggcgccg 240
 ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201
 <211> 419
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(419)
 <223> n = A,T,C or G

<400> 201
 tttttttttt ttttgaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca 60
 gctagcaagg taacagggtg gggcatggtt acatgttcag gtcaacttcc ttgtcgtgg 120
 ttgattggtt tgtctttatg gggcgggggt ggggtagggg aaancgaagc anaantaaca 180
 tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg 240
 tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatac ttttagagag 300
 tccactgtnt ctggaggagg attagggttt cttgccaana tccaancaaa atccacntga 360
 aaaagtgtga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca 419

<210> 202
 <211> 509
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 202
 tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120
 gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaattnaa 180
 tacnncnaaa aatcaaaaaa atacntntct ttcagcaaac ttngttacat aaattaaaaa 240
 aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atnttttnaa 300
 ggaactaaaa taaaaaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta 360
 caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng 420
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480
 caatggnaat nccnccnccncc tggactagt 509

<210> 203
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

<400> 203
 tttttttttt ttttttttga cccccctctt ataaaaaaca agttiaccatt ttatttttact 60
 tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac 120
 taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt 180
 gaaaatcttc tctagctctt ttgactgtaa attttttgact cttgtaaaac atccaaattc 240
 atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300
 gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360
 agggaaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc 420
 tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg 480
 tccatttttag tcaactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt 540
 attcaaaagc taatataaga tatttcacat actcatcttt ctg 583

<210> 204
 <211> 589
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(589)
 <223> n = A,T,C or G

<400> 204
 ttttttttnt tttttttttt ttttttnctt ttcttttttt ttganaatga ggatcgagtt 60
 ttctactctc tagatagggc atgaagaaaa ctcatctttc cagcttttaa ataacaatca 120
 aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc 180
 tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat 240
 tgagagggtt ttcttctcta ttacacata tatttccatg tgaatttgta tcaaaccttt 300
 attttcatgc aaactagaaa ataattgntt cttttgcata agagaagaga acaatatnag 360
 cattacaaaa ctgctcaaat tgtttgtaa gnttatccat tataattagt tnggcaggag 420
 ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc 480
 aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat 540
 ttattnagaa tgaattcaca tgttattatt ccttagccca acacaatgg 589

<210> 205
 <211> 545
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(545)
 <223> n = A,T,C or G

<400> 205
 tttttttttt ttttttccagt aataatcaga acaatattta tttttatatt taaaattcat 60
 agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120
 tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat 180
 ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt 240
 aaaaatccac tatttagcaaa taaattacta tggacttctt gcttttaatt tgtgatgaat 300
 atggggtgct actggttaac caacacattc tgaaggatac attacttagt gatagattct 360
 tatgtacttt gctatanac gtggatatga gttgacaagt ttctctttct tcaatctttt 420
 aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg 480

aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540
aacc 545

<210> 206
<211> 487
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(487)
<223> n = A,T,C or G

<400> 206
tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt 60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120
caatttataa atgtaagggt ccattattga gtanatatat tcctccaaga gtggatgtgt 180
cccttctccc accaactaat gaancagcaa cattagttaa attttattag tagatnatac 240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt 360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtggcaag 420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480
ttcaaaa 487

<210> 207
<211> 332
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(332)
<223> n = A,T,C or G

<400> 207
tgaattggct aaaagaactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa 60
tacatagcat taaatcccaa atoctattta aagacctgac agcttgagaa ggtcactact 120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana 180
atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagcgca 240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg 300
aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208
<211> 524
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(524)
<223> n = A,T,C or G

<400> 208
agggcggtgt gcggagggtg ttactgtttt gtctcagtaa caataaatac aaaaagactg 60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat 120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac 180
tcccgcgtga ttcaatttta gcaaccaaca atagctcatg agtccatact tgtaataact 240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa 300

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gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc      360
atgagcccag aactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc      420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa      480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga                        524

```

```

<210> 209
<211> 159
<212> DNA
<213> Homo sapien

```

```

<400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg      60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca      120
caaaggactc tcgacccaaa ctgcccaga ccctctcca                        159

```

```

<210> 210
<211> 256
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(256)
<223> n = A,T,C or G

```

```

<400> 210
actccctggc agacaaaggc agaggagaga gctctgtag ttctgtgttg ttgaactgcc      60
actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta      120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat      180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca      240
ccaggatgct aatca                        256

```

```

<210> 211
<211> 264
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G

```

```

<400> 211
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg      60
actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt      120
atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga      180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga      240
aaaaaggag caaatgagaa gcct                        264

```

```

<210> 212
<211> 328
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

```

75

```

<400> 212
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa      60
ggatttaaat tgtctcagc ttgggcaçtt cagttaggac ctaaggatgc cagccggcag      120
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgcag      180
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta      240
cccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca      300
tttttttttc ctttattcct ttgtcaga                                     328

```

<210> 213

<211> 250

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(250)

<223> n = A,T,C or G

```

<400> 213
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt      60
taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct      120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt      180
ttcaatatatt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct      240
tctcatcggt                                     250

```

<210> 214

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(444)

<223> n = A,T,C or G

```

<400> 214
accagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag      60
gatttaaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg      120
tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccgccagt      180
tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac      240
ccctacgact ctttactctc tggagagggc cagtgggtgg agctataagc ttggccacat      300
tttttttttc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag      360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt      420
actttgctct ccctaataata cctc                                     444

```

<210> 215

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(366)

<223> n = A,T,C or G

```

<400> 215
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt      60

```

```

taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120
cattatgcc aagganatat acatttcaat tctccaaact tcttctcat tccaagagtt 180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatt tctctgacct 240
tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa 300
tccaagctgt ttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt 360
ggtgcc

```

```

<210> 216
<211> 260
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(260)
<223> n = A,T,C or G

```

```

<400> 216
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc 60
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120
taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa 180
atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240
aattcttctt tccctccttt

```

```

<210> 217
<211> 262
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(262)
<223> n = A,T,C or G

```

```

<400> 217
acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta 60
tcttgccctat aattttctat ttttaataag aaatagcaaa ttgggggtgg gggaatgtag 120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatatt 180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta 240
atatccttca tgcttgtaaa gt 262

```

```

<210> 218
<211> 205
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(205)
<223> n = A,T,C or G

```

```

<400> 218
accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca 60
cccctatcaa ctcccttttg tagtaaaatt ggaaccttgg aaatgaccag gccaaagactc 120
aggcctcccc agttctactg acctttgtcc ttangntna ngctccagggt tgctaggaaa 180
anaaatcagc agacacaggt gtaaa 205

```

```

<210> 219

```

77

<211> 114
 <212> DNA
 <213> Homo sapien

<400> 219
 tactgttttg tctcagtaac aataaatatac aaaagactgg ttgtgttccg gcccacatcca 60
 accacgaagt tgattttctct tgtgtgcaga gtgactgatt tttaaaggaca tgga 114

<210> 220
 <211> 93
 <212> DNA
 <213> Homo sapien

<400> 220
 actagccagc acaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta 60
 aaataagcat ttagtgctca gtcctactg agt 93

<210> 221
 <211> 167
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(167)
 <223> n = A,T,C or G

<400> 221
 actangtgca ggtgcgcaca aatatttgct gatattccct tcatcttgga ttccatgagg 60
 tcttttgccc agcctgtggc tctactgtag taagtctctg ctgatgagga gccagnatgc 120
 cccccactac cttccctgac gctcccccana aatcacccaa cctctgt 167

<210> 222
 <211> 351
 <212> DNA
 <213> Homo sapien

<400> 222
 agggcggtgt gcgaggggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60
 gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120
 atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180
 ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240
 taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt 300
 ctcgatatcaa aacaatagat tggtaaagggt ggtattattg tattgataag t 351

<210> 223
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(383)
 <223> n = A,T,C or G

<400> 223
 aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60
 tggttaattat ggtcaattta atwrrtrttk ggggcatttc cttacattgt cttgacaaga 120

78

ttaaaatgtc	tgtgccaaaa	ttttgtat	tatttgaga	cttcttatca	aaagtaatgc	180
tgccaaagga	agtctaagga	attagtagtg	ttcccmcac	ttgtttggag	tgtgctattc	240
taaaagattt	tgatttcctg	gaatgacaat	tatatattta	ctttgggtggg	ggaaanagtt	300
ataggaccac	agtcttcact	tctgatactt	gtaaattaat	cttttattgc	acttggtttg	360
accattaagc	tatatgttta	aaa				383

<210> 224

<211> 320

<212> DNA

<213> Homo sapien

<400> 224

ccccgaagg	cttcttgta	gaaaatagta	cagttacaac	caataggaac	aacaaaaaga	60
aaaagtgtt	gacattgtag	tagggagtgt	gtacccctta	ctcccatca	aaaaaaaaat	120
ggatacatgg	ttaaaggata	raagggaat	attttatcat	atgttctaaa	agagaaggaa	180
gagaaaatac	tactttctcr	aaatggaagc	ccttaaaggt	gctttgatac	tgaaggacac	240
aaatgtggcc	gtccatcctc	ctttaragtt	gcatgacttg	gacacggtaa	ctgttgacgt	300
tttaractcm	gcattgtgac					320

<210> 225

<211> 1214

<212> DNA

<213> Homo sapien

<400> 225

gaggactgca	gcccgcactc	gcagccctgg	caggcggcac	tggtcatgga	aaacgaattg	60
ttctgctcgg	gcgtccctgg	gcatccgcag	tgggtgctgt	cagccgcaca	ctgtttccag	120
aactcctaca	ccatcgggct	gggcctgcac	agtcttgagg	ccgaccaaga	gccagggagc	180
cagatgggtg	aggccagcct	ctcgtacgg	caccagagt	acaacagacc	cttgctcgct	240
aacgacctca	tgctcatcaa	gttgagcgaa	tccgtgtccg	agtctgacac	catccggagc	300
atcagcattg	cttcgcagtg	ccctaccgcg	gggaactctt	gcctogtttc	tggctggggg	360
ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	tgaacgtgtc	ggtggtgtct	420
gaggaggtct	gcagtaagct	ctatgaccgg	ctgtaccacc	ccagcatggt	ctgcccgggc	480
ggagggcaag	accagaagga	ctcctgcaac	ggtgactctg	gggggcccct	gatctgcaac	540
gggtacttgc	agggccttgt	gtctttcgga	aaagcccgt	gtggccaagt	tggcgtgcca	600
ggtgtctaca	ccaacctctg	caaattcact	gagtggatag	agaaaaccgt	ccaggccagt	660
taactctggg	gactgggaac	ccatgaaatt	gacccccaaa	tacatcctgc	ggaaggaaat	720
caggaatatc	tgttcccagc	ccctcctccc	tcaggcccag	gagtccaggc	ccccagcccc	780
tcctccctca	aaccaagggt	acagatcccc	agccctcct	ccctcagacc	caggagtcca	840
gacccccag	cccctcctcc	ctcagaccga	ggagtccagc	ccctcctccc	tcagaccagc	900
gagtcacagc	ccccagcccc	ctcctccctc	agaccagggg	gtccaggccc	ccaaccctcc	960
ctccctcaga	ctcagagggt	caagccccca	accctcctt	ccccagaccc	agaggtccag	1020
gtcccagccc	ctcctccctc	agaccagcgg	gtccaatgcc	acctagactc	tcctgttaca	1080
cagtgcctcc	ttgtggcacg	ttgacccaac	cttaccagtt	ggtttttcat	tttttgtccc	1140
tttcccttag	atccagaaat	aaagtctaag	agaagcgcaa	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaa					1214

<210> 226

<211> 119

<212> DNA

<213> Homo sapien

<400> 226

accagtatg	tgcagggaga	cggaacccca	tgtgacagcc	cactccacca	gggttcccaa	60
agaacctggc	ccagtcataa	tcattcatcc	tgacagtggc	aataatcacg	ataaccagt	119

<210> 227

<211> 818

<212> DNA

<213> Homo sapien

<400> 227

acaattcata	gggacgacca	atgaggacag	ggaatgaacc	cggtctctccc	ccagccctga	60
tttttgctac	atatgggggtc	ccttttcatt	ctttgcaaaa	acactgggtt	ttctgagaac	120
acggacgggt	cttagcacia	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcctc	ctctggagga	aagggtgtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcgccct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgtcccc	ttccaatcag	ccacttctga	gaaccccat	ctaacttct	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaaggggtg	caccctcagc	agagaagccg	agagcttaac	tctggtcgtt	tccagagaca	480
acctgctggc	tgtcttgga	tgcgcccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggtgaggg	cagcaaccac	tctctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggct	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818

<210> 228

<211> 744

<212> DNA

<213> Homo sapien

<400> 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaacga	gcctcctcct	tggagatgg	aagaccgtgt	120
tcggtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
tgtcgggtgc	acattgggggt	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccaagttt	gttccactga	agcttttccc	acagcagtcc	acctctgcag	360
gctggcagct	gaatggcttg	ccgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctgggtga	cagtgaccgc	540
ccgtgggtatg	ccttgcccca	ttccagcagt	cccagttatg	catttcaagt	ttgggggttg	600
ttcttttctg	taatgttctc	ctgtgtgtgc	agctgtcttc	atttctctgg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttcactctg	aagtagctgg	tgggt				744

<210> 229

<211> 300

<212> DNA

<213> Homo sapien

<400> 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcaggggtg	ttgtttttta	attattattg	ttagaaacgt	caccacagct	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagctc	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

<210> 230

<211> 301

<212> DNA

<213> Homo sapien

<400> 230

cagcagaaca	aatacaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
------------	-----------	------------	------------	------------	------------	----

80

```

gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg 120
caatataaag tcctgggttca cactcaggaa cgagagctga cccagttaag ggagaagttg 180
cggaagggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg 240
gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgaccac 300
g 301

```

```

<210> 231
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 231
gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcatttttagc 60
caggaactcc aagtcacat ccttggcaac tggggacttg cgcaggttag ccttgaggat 120
ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180
tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240
tttttttggtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300
c 301

```

```

<210> 232
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 232
agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagttctcc ttcaagtgtt 60
ggcgacacgc gggcttcctg attctggaat ataactttgt gtaaattaac agccacctat 120
agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca 180
cgtgctgtac caagtgctgg tgccagcctg ttacctgttc tctactgaaa tctggctaatt 240
gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
g 301

```

```

<210> 233
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 233
atgactgact tcccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag 60
atgctaaggc cccagagatc gtttgatcca accctcttat ttccagaggg gaaaatgggg 120
cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180
gagtagctgg gactacaggg acacagtcac tgaagcaggc cctgttagca attctatgcg 240
tacaatttaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300
c 301

```

```

<210> 234
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 234
aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60
cattttattc atcatgatgc tttcttttgt ttcttctttt cgttttcttc tttttctttt 120
tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180
cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgc 240
ttgatcacca gcttaatggt cagatcatct gttcaatgg cttcgtcagt atagtcttc 300
t 301

```

81

<210> 235
 <211> 283
 <212> DNA
 <213> Homo sapien

<400> 235
 tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg 60
 aattccctca tcttttaggg aatcatttac caggtttga gaggattcag acagctcagg 120
 tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata 180
 atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca 240
 ttagggattc aaagaaatat tagatttaag ctcacactgg tca 283

<210> 236
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 236
 aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata 60
 aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg 120
 tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggatatatag 180
 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta 240
 aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300
 a 301

<210> 237
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 237
 cagtggtagt ggtggtggac gtggcggttg tctgtgtgcc ttttttggtg cccgtcacia 60
 actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg 120
 ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct 180
 ttgggtagtt ggtgccaagc tctgcaatgg cacagaatgg atcagcttct cgtaaatacta 240
 ggggtccgaa attctttctt cctttggata atgtagtcca tatccattcc ctcttttacc 300
 t 301

<210> 238
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 238
 gggcagggtt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt 60
 gttcacagtt cagccccctg ctcaaaaaac caacgggcca gctaaggaga ggaggaggca 120
 ccttgagact tccggagtcg aggtctctca gggttcccca gcccatcaat cattttctgc 180
 accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240
 gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300
 t 301

<210> 239
 <211> 239
 <212> DNA
 <213> Homo sapien

<400> 239
 ataagcagct aggggaattct ttatttagta atgtcctaac ataaaagttc acataactgc 60

ttctgtcaaa	ccatgatact	gagctttgtg	acaaccaga	aataactaag	agaaggcaaa	120
cataatacct	tagagatcaa	gaaacattta	cacagttcaa	ctgttttaaaa	atagctcaac	180
attcagccag	tgagtagagt	gtgaatgcca	gcatacacag	tatacaggtc	cttcaggga	239

<210> 240
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 240						
gggtcctaag	aagcagcagc	ttccacattt	taacgcaggt	ttacgggtgat	actgtccttt	60
gggatctgcc	ctccagtggg	accttttaag	gaagaagtgg	gccaagcta	agttccacat	120
gctgggtgag	ccagatgact	tctgttcctt	gtcacttttc	ttcaatgggg	cgaatggggg	180
ctgccagggt	tttaaaatca	tgcttcatct	tgaagcacac	ggtcacttca	ccctcctcac	240
gctgtgggtg	tactttgatg	aaaataccca	ctttgttggc	ctttctgaag	ctataatgtc	300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241						
gaggtctggt	gctgaggtct	ctgggctagg	aagaggagtt	ctgtggagct	ggaagccaga	60
cctcttttga	ggaaactcca	gcagctatgt	tggtgtctct	gagggaatgc	aacaaggctg	120
ctcctccatg	tattggaaaa	ctgcaaaactg	gactcaactg	gaaggaagtg	ctgctgccag	180
tgtgaagaac	cagcctgagg	tgacagaaac	ggaagcaaac	aggaacagcc	agtcttttct	240
tcctcctcct	gtcatacggg	ctctctcaag	catcctttgt	tgtcaggggc	ctaaaaggga	300
g						301

<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242						
ccgaggtcct	gggatgcaac	caatcactct	gtttcacgtg	acttttatca	ccatacaatt	60
tgtggcattt	cctcattttc	tacattgtag	aatcaagagt	gtaaaataat	gtatatcgat	120
gtcttcaaga	atatatcatt	cctttttcac	tagaaccat	tcaaaatata	agtcaagaat	180
cttaatatca	acaaatata	caagcaaact	ggaaggcaga	ataactacca	taatttagta	240
taagtaccca	aagttttata	aatcaaaagc	cctaatagata	accattttta	gaattcaatc	300
a						301

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243						
aggtaagtcc	cagtttgaag	ctcaaaagat	ctggtatgag	cataggctca	tcgacgacat	60
gggtggccaa	gctatgaaat	cagagggagg	cttcactctg	gcctgtaaaa	actatgatgg	120
tgacgtgcag	tcggactctg	tgcccaagg	gtatggctct	ctcggcatga	tgaccagcgt	180
gctggtttgt	ccagatggca	agacagtaga	agcagaggct	gccacggga	ctgtaaccgg	240
tcactaccgc	atgttccaga	aaggacagga	gacgtccacc	aatcccattg	cttccatttt	300
t						301

<210> 244
 <211> 300
 <212> DNA

<213> Homo sapien

<400> 244

gctggtttgc	aagaatgaaa	tgaatgattc	tacagctagg	acttaacctt	gaaatggaaa	60
gtcatgcaat	cccatttgca	ggatctgtct	gtgcacatgc	ctctgtagag	agcagcattc	120
ccagggacct	tggaacagct	tgacactgta	agggtgcttg	tccccaagac	acatcctaaa	180
agggtgttga	atggtgaaaa	cgtcttcctt	ctttattgcc	ccttcttatt	tatgtgaaca	240
actgtttgtc	ttttgtgtat	cttttttaaa	ctgtaaagtt	caattgtgaa	aatgaatatc	300

<210> 245

<211> 301

<212> DNA

<213> Homo sapien

<400> 245

gtctgagtat	ttaaaatggt	attgaaatta	tccccaacca	atgttagaaa	agaaagaggt	60
tatatactta	gataaaaaat	gagggtgaatt	actatccatt	gaaatcatgc	tcttagaatt	120
aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	cactcaatac	240
agctaataaa	atgaaagacc	taattttctaa	agcaattctt	tataatttac	aaagttttaa	300
g						301

<210> 246

<211> 301

<212> DNA

<213> Homo sapien

<400> 246

ggtctgtcct	acaatgcctg	cttcttgaaa	gaagtcggca	ctttctagaa	tagctaaata	60
acctgggctt	attttaaaga	actatttgta	gtcagatttg	gttttcctat	ggctaaaata	120
agtgtctctt	gtgaaaatta	aataaaacag	ttaattcaaa	gccttgatat	atgttaccac	180
taacaatcat	actaaatata	ttttgaagta	caaagtttga	catgctctaa	agtgacaacc	240
caaagtgtgc	ttacaaaaca	cgttcctaac	aagggtatgct	ttacactacc	aatgcagaaa	300
c						301

<210> 247

<211> 301

<212> DNA

<213> Homo sapien

<400> 247

aggctccttg	gcagggtcct	tggatcagag	ctcaaactgg	agggaaggc	atttcgggta	60
gcctaagagg	gcgactggcg	gcagcacaac	caagggaaggc	aagggtgttt	ccccacgct	120
gtgtcctgtg	ttcagggtgcg	acacacaatc	ctcatgggaa	caggatcacc	catgcgctgc	180
ccttgatgat	caagggtggg	gcttaagtgg	attaaggagg	gcaagttctg	ggttccttgc	240
cttttcaaac	catgaagtca	ggctctgtat	ccctcctttt	cctaactgat	attctaacta	300
a						301

<210> 248

<211> 301

<212> DNA

<213> Homo sapien

<400> 248

aggctccttg	agatgccatt	tcagccgaag	gactcttctw	ttcggaagta	caccctcact	60
attaggaaga	ttcttagggg	taatttttct	gagggaaggag	aactagccaa	cttaagaatt	120
acaggaagaa	agtggtttgg	aagacagcca	aagaaataaa	agcagattaa	attgtatcag	180
gtacattcca	gcctgttggc	aactccataa	aaacatttca	gatttttaac	ccgaatttag	240

ctaagtacac tggatTTTTG ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300
c 301

<210> 249
<211> 301
<212> DNA
<213> Homo sapien

<400> 249
gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag 60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgccc 120
ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc 180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt 300
a 301

<210> 250
<211> 301
<212> DNA
<213> Homo sapien

<400> 250
ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc 60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc 120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac 180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta 240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300
a 301

<210> 251
<211> 301
<212> DNA
<213> Homo sapien

<400> 251
gccgaggtcc tacatttggc ccagtttccc cctgcacact ctccagggcc cctgcctcat 60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat 120
ggcaggggtc ctcaaaaatg ccaactgtcac tgccaggaaa tgcttctgag cagtacacct 180
cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgaa 240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct 300
c 301

<210> 252
<211> 301
<212> DNA
<213> Homo sapien

<400> 252
gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttctca 60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata 120
tcatttcctt ttacttagga acccattcaa aatataagtc aagaatctta atatcaaaa 180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt 240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300
a 301

<210> 253
<211> 301
<212> DNA

85

<213> Homo sapien

<400> 253

```
ttccctaaga agatgttatt ttgttgggtt ttgttcccc tccatctcga ttctcgtacc    60
caactaaaaa aaaaaataaa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct    120
tggtctgatt gttttcagac cttaaaatat aaacttggtt cacaagcttt aatccatgtg    180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt    240
tccatagtgc ccacagggta ttcttcacat tttctccata ggaaatgct ttttcccaag    300
g                                           301
```

<210> 254

<211> 301

<212> DNA

<213> Homo sapien

<400> 254

```
cgctgcgcct ttcccttggg ggagggggcaa ggccagaggg ggtccaagtg cagcacgagg    60
aacttgacca attcccttga agcgggtggg ttaaaccttg taaatgggaa caaaatcccc    120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa    180
gaaaaaataa aagctttgga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc    240
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc    300
t                                           301
```

<210> 255

<211> 302

<212> DNA

<213> Homo sapien

<400> 255

```
agcttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa    60
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat    120
tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg    180
aggaaaaagg actggagggt gaatctttat aaaaaacaag agtgattgag gcagattgta    240
aacattatta aaaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac    300
aa                                           302
```

<210> 256

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 256

```
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct    60
aggacctctc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc    120
acccccaaaa gcctggacac cttgagcaca cagttagtac caggacagac tcactcttat    180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt    240
gtggcctctc ggctgggtta gcaagaacat tcagggtagg cctaagttaa tcgtgttagt    300
t                                           301
```

<210> 257

<211> 301

<212> DNA

<213> Homo sapien

<400> 257						
gttgtggagg	aactctggct	tgctcattaa	gtcctactga	ttttcactat	ccctgaatt	60
tcccaccta	tttttgcctt	tcactatcgc	aggccttaga	ataggctctac	ctgcctccag	120
ttccacttag	tcaggtctac	cccttgga	tagaatggcc	atcctgaagt	gaaaagtaat	180
gtcacattac	tcccttcagt	gatttcttgt	agaagtgcc	atccctgaat	gccaccaaga	240
ttctaatctt	cacatcttta	atcttatctc	tttgactcct	ctttacaccg	gagaaggctc	300
c						301

```
<210> 258
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
```

<400> 258						
cagcagtagt	agatgccgta	tgccagcacg	cccagcactc	ccaggatcag	caccagcacc	60
aggggccag	ccaccaggcg	cagaagcaag	ataaacagta	ggctcaagac	cagagccacc	120
cccagggcaa	caagaatcca	ataccaggac	tgggcaaaat	cttcaaagat	cttaacactg	180
atgtctcggg	cattgaggct	gtcaataana	cgctgatccc	ctgctgtatg	gtggtgtcat	240
tggtgatccc	tgggagcgcc	ggtggagtaa	cgttggtcca	tggaaagcag	cgcccacaac	300
t						301

```
<210> 259
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
```

<400> 259						
tcatatatgc	aaacaaatgc	agactangcc	tcaggcagag	actaaaggac	atctcttggg	60
gtgtcctgaa	gtgatttggc	cccctgagg	cagacaccta	agttaggaac	ccagtggtgaa	120
gc aaagcat	aaggaagccc	aggatttcct	gtgatcagga	agtggggccag	gaaggtctgt	180
tccagctcac	atctcatctg	catgcagcac	ggaccggatg	cgcccaactg	gtcttggctt	240
ccctcccatc	ttctcaagca	gtgtccttgt	tgagccattt	gcacctcttg	ctccaggtgg	300
c						301

```
<210> 260
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 260						
ttttttttct	ccctaaggaa	aaagaaggaa	caagtctcat	aaaaccaa	aagcaatgg	60
aaggtgctt	aacttgaaa	agattaggag	tcactggtt	acaagttata	attgaatgaa	120
agaactgtaa	cagccacagt	tggccatttc	atgccaatgg	cagcaaaaca	caggatataac	180
tagggcaaaa	taaataagtg	tgtggaagcc	ctgataaagt	cttaataaac	agactgattc	240
actgagacat	cagtacctgc	cggggcggcc	gctcgagccg	aattctgcag	atatccatca	300
C						301

87

<210> 261
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 261
 aaatattcga gcaaatacctg taactaatgt gtctccataa aaggctttga actcagtgaa 60
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggtt 120
 agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggttcaat 180
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240
 ggcatgatga tcatccaaag ccagtggtc acttactcca gactttctgc aatgaagatc 300
 a 301

<210> 262
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 262
 gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatacc ctgagtcacc 120
 cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgtccc 240
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300
 c 301

<210> 263
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 263
 tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60
 aaaattacta cttaatccta attcacaata acaatggcat taagggttga cttgagttgg 120
 ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180
 taatgactga cttcccagta aggtctctta aggggtaagt angaggatcc acaggatttg 240
 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300
 g 301

<210> 264
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 264
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60
 aatgaatgac tctaaaaaca atattttacat ttaatgggtt gtagacaata aaaaaacaag 120
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
 acccttcata taaattcact atcttggcct gaggcactcc ataaaatgta tcacgtgcat 300
 a 301

<210> 265

88

<211> 301
 <212> DNA
 <213> Homo sapien

<400> 265
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcattctttgt 60
 cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120
 catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga 180
 ttttcagttt gtcaacatgt tctctaaca cacttgccca tttctgtaaa gaatccaaag 240
 cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300
 c 301

<210> 266
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 266
 taccgtctgc ccttcctccc atccaggcca tctgcgaatc tacatgggtc ctcctattcg 60
 acaccagatc actctttcct ctaccacag gcttgctatg agcaagagac acaacctcct 120
 ctcttctgtg ttccagcttc ttttctgtt cttcccaccc ctttaagttct attcctgggg 180
 atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca ggggtgcacag 240
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg 300
 a 301

<210> 267
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 267
 aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg 60
 gttctcagtg ctgagtccat ccaggaaaag ctcacctaga ctttctgagg ctgaatcttc 120
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatggctt ggagtaaagc 180
 ctcattctga ttctctctct tcttttcttt caagttggct ttctcacat ccctctgttc 240
 aattcgcttc agcttgtctg ctttagccct catttccaga agcttcttct ctttggcctc 300
 t 301

<210> 268
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 268
 aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta 60
 gatcttggga gagctgggtc ttctaaggag aaggagggaag gacagatgta actttggatc 120
 tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttgggaata 180
 tgctgggtgg ctcagtgagc ccttttggag aaagcaagta ttattcttaa ggagtaacca 240
 cttccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact 300
 a 301

<210> 269
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 269
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60

89

```

aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact    120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta    180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta    240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc    300
t                                                                    301

```

```

<210> 270
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgcct ataaaattaa ttaagcctta    60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga    120
gagcttgctg gtgcagtgc tattggataa cactattcat ggccgaattg atcaagtcaa    180
ccaactcctt gaactggatc atcagaagaa ggggtgtgca cgatatactg cactagataa    240
tggaaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcct aacagaaaac    300
a                                                                    301

```

```

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 271
aaaagggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt    60
tttatagctc atctttaggg ttgatattca gttcatgcct cccttgctgt tottgatcca    120
gaattgcaat cacttcacga gcctgtatcc gctccaattc tctataaagt gggccaagg    180
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt    240
tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca    300
c                                                                    301

```

```

<210> 272
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc    60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga    120
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacctctcc tgcattccaca    180
gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc    240
ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag    300
g                                                                    301

```

```

<210> 273
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)

```

<223> n = A, T, C or G

<400> 273

acatgtgtgt	atgtgtatct	ttgggaaaaan	aanaagacat	cttgtttayt	atTTTTTTgg	60
agagangctg	ggacatggat	aatcacwtaa	tttgctayta	tyactttaat	ctgactygaa	120
gaaccgtcta	aaaataaaat	ttaccatgtc	dtatatcct	tatagtatgc	ttatttcacc	180
ttytttctgt	ccagagagag	tatcagtgac	ananatttma	gggtgaamac	atgmattggt	240
gggaacttnty	tttacngagm	accctgcccg	sgcgccctcg	makcngantt	ccgcsananc	300
t						301

<210> 274

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

 $\langle 222 \rangle \quad (1) \dots (301)$

<223> n = A, T, C or G

<400> 274

cttatataact	ctttctcaga	ggcaaaagag	gagatgggta	atgtagacaa	ttctttgagg	60
aacagtaaat	gattattaga	gagaangaat	ggaccaagga	gacagaaatt	aacttgtaaa	120
tgattctctt	tggaatctga	atgagatcaa	gaggccagct	ttagcttgty	gaaaagtcca	180
tctaggtatg	gttgcatctt	cgtcttcttt	tctgcagtag	ataatgaggt	aaccgaaggc	240
aatttgtgctt	cttttgataa	gaagctttct	tggtcatatc	aggaaattcc	aganaaaagtc	300
c						301

<210> 275

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

$\langle 222 \rangle$ (1) ... (301)

<223> n = A, T, C or G

<400> 275

tcggtgtcag	cagcacgtgg	cattgaacat	tgcaatgtgg	agcccaaacc	acagaaaatg	60
gggtgaaatt	ggccaacttt	ctattaactt	atgttgccaa	ttttgccacc	aacagtaagc	120
tggcccttct	aataaaagaa	aattgaaag	tttctacta	aacggaatta	agtagtgag	180
tcaagagact	cccaggcctc	agcgtaacctg	ccggggcggc	cgctcgaagc	cgaattctgc	240
agatatccat	cacactggcg	gncgctcgan	catgcatcta	gaaggnccaa	ttcgccctat	300
a						301

<210> 276

<211> 301

<212> DNA

<213> Homo sapien

<400> 276

tgtagacata	ctcaataaat	aatgactgc	attgtggtat	tattactata	ctgattatat	60
ttatcatgtg	acttctaatt	agaaaatgta	tccaaaagca	aaacagcaga	tatacaaat	120
taaagagaca	gaagatagac	attaacagat	aaggcaactt	atacattgag	aatccaaatc	180
caatacattt	aaacatttgg	gaaatgaggg	ggacaaatgg	aagccagatc	aaatttgtgt	240
aaaactattc	agtatgtttc	ccttgcttca	tgtctgagaa	ggctctcctt	caatggggat	300
g						301

<210> 277
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 277
tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctgga aattctaaag 60
atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120
gaatcatggc actcctgata ctttcccaa tcaacactct caatgcccc ccctcgtcct 180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240
gttcnctgtc gattacatct gaccagtctc ctttttcoga agtccntccg ttcaatcttg 300
c 301

<210> 278
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 278
taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60
aacatatcaa atgaacacag gaaaatgaag ctgacaattt atggaagcca gggcttgta 120
cagtctctac tggtattatg cattacctgg gaatttata aagcccttaa taataatgcc 180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgtc tcacagggtt 240
tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300
c 301

<210> 279
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 279
aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60
gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120
ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300
a 301

<210> 280
<211> 301
<212> DNA

<213> Homo sapien

<400> 280

ggtactggag	ttttcctccc	ctgtgaaaac	gtaactactg	ttgggagtga	attgaggatg	60
tagaaagggtg	gtggaaccaa	atttgtgtca	atggaaatag	gagaatatgg	ttctcactct	120
tgagaaaaaa	acctaagatt	agcccaggta	gttgccctgta	acttcagttt	ttctgcctgg	180
gtttgatata	gtttaggggt	ggggtttagt	taagatctaa	attacatcag	gacaaagaga	240
cagactatta	actccacagt	taattaagga	ggtaggttcc	atgtttattt	gttaaagcag	300
t						301

<210> 281

<211> 301

<212> DNA

<213> Homo sapien

<400> 281

aggtacaaga	aggggaatgg	gaaagagctg	ctgctgtggc	attgttcaac	ttggatatcc	60
gccgagcaat	ccaaatcctg	aatgaagggg	catcttctga	aaaaggagat	ctgaatctca	120
atgtggtagc	aatggcttta	tcgggttata	cggatgagaa	gaactccctt	tgagagagaa	180
tgtgtagcac	actgcgatta	cagctaaata	acccgtatct	gtgtgtcatg	tttgcatctc	240
tgacaagtga	aacaggatct	tacgatggag	ttttgtatga	aaacaaagtt	gcagtacctc	300
g						301

<210> 282

<211> 301

<212> DNA

<213> Homo sapien

<400> 282

cagggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tccagaaccc	aaaaattaag	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagcccag	gcagaacctt	gctaacctta	cagctcagcc	tgacacagaag	180
cgcagaagca	aagcccaggc	agaacctatg	taaccttaca	gctcagcctg	cacagaagcg	240
cagaagcaaa	gcccaggcag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

<210> 283

<211> 301

<212> DNA

<213> Homo sapien

<400> 283

atctgtatac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaag	60
cacttttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggtgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaattttgtt	aaattctata	atgggtgatat	gcattcttta	240
ggaaacatat	acatttttaa	aaatctatct	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

<210> 284

<211> 301

<212> DNA

<213> Homo sapien

<400> 284

cagggtacaaa	acgctattaa	gtggccttaga	atttgaacat	ttgtggctctt	tatttacttt	60
gcttcgtgtg	tgggcaaaag	aacatcttcc	ctaaatatat	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacagg	ccaaaagggg	gctgacctgg	agcagagcat	180

93

```

ggtgagaggc aaggcatgag agggcaagtt tggttgggac agatctgtgc ctactttatt 240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt 300
a 301

```

<210> 285

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 285

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acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
caggaaagca aatgctatatt acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
attaaatatg tctgacttct tttgagggtca cagcactagg caaatgctat ttacgatctg 240
caaaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300
t 301

```

<210> 286

<211> 301

<212> DNA

<213> Homo sapien

<400> 286

```

taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60
tgtatattat ttttgccctta cagtggatca ttctagtagg aaaggacagt aagatTTTTT 120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccaccca 180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240
gtttctgttc attgtgtatg cttcatcacc tatatttaggc aaattccatt tttcccttg 300
t 301

```

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<400> 287

```

tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120
aaatgatttg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc 180
ccgtggttat ctctcccca gcttggtgc ctcattgtat cacagtattc cattttgttt 240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300
t 301

```

<210> 288

<211> 301

<212> DNA

<213> Homo sapien

<400> 288

```

gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120
gatcttttaa gcacatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180
aaaagcatct gcttttgtga tttaatttag ctcactctgg cactggaaga atccaaacag 240

```

tctgccttaa ttttgatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300
a 301

<210> 289
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 289
ggtacactgt ttccatgta tgtttctaca cattgctacc tcagtgtcc tggaaactta 60
gcttttgatg totccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga 240
tgtgtttgt tttgactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga 300
a 301

<210> 290
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 290
aactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60
tgactgatct gttcatttct ctacagctc ttaccccaa aagcttttcc accctaagtg 120
ttctgacctc tttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg cttagcagtc 240
tgcttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagttag 300
a 301

<210> 291
<211> 301
<212> DNA
<213> Homo sapien

<400> 291
caggtaacaa tttcttctat cctagaaaca tttcatttta tgttggtgaa acataacaac 60
tataacagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180
agccatggct gtttacttca ttaattttat ttagcataaa gacattatga aaaggcctaa 240
acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct 300
a 301

<210> 292
<211> 301
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 292
 accttttagt agtaatgtct .aataataaat aagaaatcaa ttttataagg tccatatagc 60
 tgtattaaat aatttttaag tttaaaagat aaaataccat catttttaaat gttggtattc 120
 aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg 180
 ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc 240
 tcactacaca cacagacccc acagtccctat atgccacaaa cacatttcca taacttgaaa 300
 a 301

<210> 293
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 293
 ggtaccaagt gctggtgccg gcctgttacc tgttctcact gaaaagtctg gctaagtctc 60
 ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactggt 120
 aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt 180
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg 240
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcgggc gctcgagcat 300
 g 301

<210> 294
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 294
 tgaccataaa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag 60
 attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag 120
 tttaactata gtcacaganc ttaaaatatt acattgtttt ctatgtctac tgaaaataag 180
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240
 cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt 300
 t 301

<210> 295
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 295
 gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta 60
 cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttggt aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180
 actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg tttaataaat tagtttgggt 300
 tctct 305

<210> 296
 <211> 301

<212> DNA

<213> Homo sapien

<400> 296

```

aggtagctatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct    60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg    120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac    180
tttgaanaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt    240
tgtcattact ataaatttta aaatctgtta ataagatggc ctataggagg gaaaaagggg    300
c

```

<210> 297

<211> 300

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(300)

<223> n = A,T,C or G

<400> 297

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actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgctcta    60
aagggttttg aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga    120
acaaagangt gaaccagctg aaagctctcg ggggaancct acatgtgttg ttaggcctgt    180
tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtgggc    240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg    300

```

<210> 298

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 298

```

tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg    60
ggcatctgag agacctggtg ttccagtgtt tctgaaaatg ggtcccagtg ccgccggctg    120
tgaagctctc agatcaatca cgggaagggc ctggcgggtg tggccacctg gaaccaccct    180
gtcctgtctg tttacatttc actaycaggt tttctctggg cattacnatt tgttccccta    240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg    300
t

```

<210> 299

<211> 301

<212> DNA

<213> Homo sapien

<400> 299

```

gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggctctctgc    60
tcaactgcacc ctctgcctcc caggtttcgag caattctcct gcctcagcct cccaggtagc    120
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg    180
gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct    240
cggcctcca aagtgtctgga attataggca tgagtcaaca cgcccagcct aaagatatatt    300
t

```

97

<210> 300
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 300
 attcagtttt atttgcctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60
 tatgtccac acccactggg aaaggctccc acctggctac ttctctatc agctgggtca 120
 gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta 180
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac 240
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat 300
 g 301

<210> 301
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 301
 ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120
 gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaagacc 180
 ctgagagctg agacaccac aacagtggga gtcacaaaag accctcagag ctgagacacc 240
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300
 t 301

<210> 302
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 302
 aggtacacat ttagcttgtg gtaaagtact cacaaaactg attttaaaat caagttaatg 60
 tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120
 ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300
 g 301

<210> 303
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 303
 aggtaccaac tgtggaaata ggtagaggat catTTTTtct ttccatatca actaagttgt 60
 atattgtttt ttgacagttt aacacatctt cttctgtcag agattcttct acaatagcac 120
 tggctaattg aactaccgct tgcatgttaa aaatgggtgt ttgtgaaatg atcataggcc 180
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240
 catcgatttt atatctgggg totagaaaag gagttaatct gttttccctc ataaattcac 300
 c 301

<210> 304
 <211> 301
 <212> DNA
 <213> Homo sapien

98

<400> 304
 acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaatt 60
 tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc 120
 ctttttagtg tatcatatca ggaatcatct cacattgggtt tgtgccatta ctggtgcagt 180
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240
 ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300
 c 301

<210> 305
 <211> 301
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 305
 gangtacagc gtgggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60
 caggggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120
 taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180
 aatatttgta gaaacaagaa tacattcata tggcaataaa ctaaccatgg tggaacaaaa 240
 ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300
 a 301

<210> 306
 <211> 8
 <212> PRT
 <213> Homo sapien

<400> 306
 Val Leu Gly Trp Val Ala Glu Leu
 1 5

<210> 307
 <211> 637
 <212> DNA
 <213> Homo sapien

<400> 307
 acaggggratg aagggaag gagaggatga ggaagcccc ctggggattt ggtttgggtcc 60
 ttgtgatcag gtggtctatg gggcttatcc ctacaagaa gaatccagaa atagggggcac 120
 attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180
 cacaccattg gtgaggagg gattaccacc ctggggttat gaagatggtt gaacacccca 240
 cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300
 gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360
 aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacgggtggg caaactctga 420
 tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480
 actcattagg ctgagaacct tgtggaatgc acttgacca sctgatatag gaagtagcca 540
 ggtggggagcc tttccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600
 ttacagatac tggggcagca aataaaactg aatcttg 637

<210> 308
 <211> 647
 <212> DNA
 <213> Homo sapien

99

<220>
 <221> misc_feature
 <222> (1)...(647)
 <223> n = A,T,C or G

<400> 308
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60
 tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa 120
 gngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180
 ccacccctct gacccttttg aactcctctg accctttaga acaagcctac ctaatatctg 240
 ctagagaaaa gaccaacaac ggctcaaag gatctcttac catgaaggtc tcagctaatt 300
 cttggctaag atgtgggttc cacattaggc tctgaatatg gggggaagg tcaatttgct 360
 cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 420
 gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480
 tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 540
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309
 <211> 460
 <212> DNA
 <213> Homo sapien

<400> 309
 actttatagt ttaggtgga cattggaaaa aaaaaaagc cagaacaaca tgtgatagat 60
 aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180
 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtcag 240
 ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctaccag 300
 ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggttaacc 360
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 420
 ttgtcttggt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310
 <211> 539
 <212> DNA
 <213> Homo sapien

<400> 310
 acgggactta tcaaataaag ataggaaaag aagaaaactc aaatattata ggcagaaatg 60
 ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 120
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180
 gtcagacagt aagattttgtg ggaatgggt tggtttgttg tatggtatgt attttagcaa 240
 taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa 300
 ttctcgaagg taggcatgat gaaggagggt tttagaggaga cacagacaca atgaactgac 360
 ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc aactgtgac 420
 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaa aacttatggc 480
 atattttcac ccccaaaaa gtcagttaaa tattgggaca ctaacctcc aggtcaaga 539

<210> 311
 <211> 526
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(526)
 <223> n = A,T,C or G

100

<400> 311

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ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	atttaaatg	tggtcagcat	gaaatattag	ctacagggga	agctaaataa	180
attaacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggctgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	cctttttagt	atctgtgtat	caagtataaa	480
agttctataa	actgtagtnt	acttatttta	atccccaag	cacagt		526

<210> 312

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(500)

<223> n = A,T,C or G

<400> 312

cctctctctc	cccacccct	gactctagag	aactgggttt	tctcccagta	ctccagcaat	60
tcattttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccattttctct	ttcccttcca	cctgccagtt	ttgtcgactc	tcaacttgct	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atccccctct	300
tgcagatgtc	tagcagcttc	agacatttgg	ttaagaacct	atgggaaaaa	aaaaaatcct	360
tgctaagtgt	gtttcctttg	taaaccanga	ttcttatttg	nctggatatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aatcagttt	gctgaaaagt	480
tagtcttaat	tatctatttg					500

<210> 313

<211> 718

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(718)

<223> n = A,T,C or G

<400> 313

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tgatgataca	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataaatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgacat	gtttttgcac	atttccagcc	cttttaata	tccacacaca	caggaagcac	240
aaaaggaagc	acagagatcc	ctgggagaaa	tgcccggccg	ccatcttggg	tcacgatga	300
gcctcgccct	gtgcctgntc	ccgcttgtga	gggaaggaca	ttagaaaatg	aattgatgtg	360
ttccttaaaag	gatggcagga	aaacagatcc	tggtgtggat	atttatttga	acgggattac	420
agatttgaaa	tgaagtcaca	aagtgagcat	taccaatgag	aggaaaacag	acgagaaaat	480
cttgatggtt	cacaagacat	gcaacaaaca	aaatggaata	ctgtgatgac	acgagcagcc	540
aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
ogttatacca	atcatttcta	tttctaccct	caaacagct	gtngaataac	tgacttacgg	660
ttcttntggc	ccacattttc	atnatccacc	ccntcntttt	aannttantic	caaantgt	718

<210> 314

101

<211> 358
 <212> DNA
 <213> Homo sapien

<400> 314
 gtttattttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata 60
 cataatcaaaa tatagctgta gtacatgttt tcattgggtg agattaccac aaatgcaagg 120
 caacatgtgt agatctcttg tcttatttctt ttgtctataa tactgtattg tgtagtccaa 180
 gctctcggta gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc 240
 ttgttggtatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttgct 300
 tctggggcat ttccttggtga tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315
 <211> 341
 <212> DNA
 <213> Homo sapien

<400> 315
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 ataggtgatg atgaggacat ggaatgggcc cccaaggatg gtctgtccaa agaagcgagt 120
 gaccccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac 180
 agtcaccagc tccccgacca gccggatata gtccttaggg gtcatgtagg cttcctgaag 240
 tagcttctgc tgtaagaggg tgtgtccccg ggggctcgtg cggttattgg tctgggctt 300
 gaggggggcgg tagatgcagc acatgggtgaa gcagatgatg t 341

<210> 316
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 316
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 tgtgggctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120
 cattcaggga gctctggttg caatattagt t 151

<210> 317
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 317
 agaactagt gatcctaag aaataacctga aacatatatt ggcatttatc aatggctcaa 60
 atcttcattt atctctggcc ttaaccttgg ctcctgaggg tgcggccagc agatcccagg 120
 ccagggtctt gttcttgcca cacctgcttg a 151

<210> 318
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 318
 actggtggga ggcgctgttt agttggctgt tttcagaggg gtctttcgga gggacctcct 60
 gctgcaggct ggagtgttt tattcctggc gggagaccgc acattccact gctgaggctg 120
 tggggggcgt ttatcaggca gtgataaaca t 151

<210> 319
 <211> 151
 <212> DNA

102

<213> Homo sapien

<400> 319

aactagtggga tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta	60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg	120
taagattggg tttatgtgat tttagtgggt a	151

<210> 320

<211> 150

<212> DNA

<213> Homo sapien

<400> 320

aactagtggga tccactagtc cagtgtgggt gaattccatt gtgttggggt tctagatcgc	60
gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt	120
gagtgttcta cagcttacag taaataccat	150

<210> 321

<211> 151

<212> DNA

<213> Homo sapien

<400> 321

agcaactttg tttttcatcc aggttatattt aggccttagga tttcctctca cactgcagtt	60
taggggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg	120
tgctctgag aaatcaaagt ctccatacac t	151

<210> 322

<211> 151

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(151)

<223> n = A,T,C or G

<400> 322

atccagcatc ttctcctggt tcttgccctc cttttcttc ttcttasatt ctgcttgagg	60
tttgggcttg gtcagtttgc cacagggctt ggagatgggt acagtcttct ggcattcggc	120
attgtgcagg gctcgcttca nacttcagtt t	151

<210> 323

<211> 151

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(151)

<223> n = A,T,C or G

<400> 323

tgaggacttg tktttttttt cttttttttt aatcctctta ckttgtaaatt atattgccta	60
nagactcant tactaccag tttgtggttt twtgggagaa atgtaactgg acagttagct	120
gttcaatyaa aaagacactt ancccatgtg g	151

<210> 324

103

<211> 461
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(461)
 <223> n = A,T,C or G

<400> 324
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 agaagtggc agctaaagga atccagggtg ttggttgac tgtaataacc tttgatgaaa 120
 agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact 180
 gcgaacctca cttctagact ttacaggtgg gacgaaacgg gttcagaaac tgccaggggc 240
 ctcatcacgg gatatacaaa taccctttgt gctaccagg ccctggggaa tcagggtgact 300
 cacacaaatg caatagttgg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt 360
 gccaccatgc accatggcat gccagagttc aacactggtg ctcttgaaaa ttgggtctga 420
 aaaaacgcac aagagcccct gccctgccct agctgangca c 461

<210> 325
 <211> 400
 <212> DNA
 <213> Homo sapien

<400> 325
 acaactgtttc catgttatgt ttctacacat tgctacctca gtgctcctgg aaacttagct 60
 tttgatgtct ccaagtagtc caccttcatt taactctttg aaactgtatc atctttgcc 120
 agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt 180
 tctataaatg aatgtgctga agcaaatg ccatgggtggc ggcaagaag agaaagatgt 240
 gttttgtttt ggactctctg tggctccctc caatgctgtg gggttccaac caggggaagg 300
 gtcccttttg cattgccaa tgccataacc atgagcacta cgctaccatg gttctgcctc 360
 ctggccaagc aggttggttt gcaagaatga aatgaatgat 400

<210> 326
 <211> 1215
 <212> DNA
 <213> Homo sapien

<400> 326
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 gttctgctcg ggcgtcctgg tgcacccgca gtgggtgctg tcagccgcac actgtttcca 120
 gaactcctac accatcgggc tgggcctgca cagtcttgag gccgaccaag agccaggagg 180
 ccagatggtg gaggccagcc tctccgtacg gcacccagag tacaacagac ccttgctcgc 240
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 catcagcatt gcttcgcagt gccctaccgc ggggaactct tgcctcgttt ctggctgggg 360
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 cgggtacttg cagggccttg tgtctttcgg aaaagccccg tgtggccaag ttggcgtgcc 600
 aggtgtctac accaacctct gcaaattcac tgagtggata gagaaaaccg tccaggccag 660
 ttaactctgg ggaactggaa cccatgaaat tgaccccaa atacatcctg cggaaggaaat 720
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 ctctccctc aaaccaaggg tacagatccc cagccctcc tccctcagac ccaggagtcc 840
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 gggtccagcc cctcctccct cagaccagc ggtccaatgc cacctagact ctccctgtac 1080
 acagtgcacc cttgtggcac gttgacccaa ccttaccagt tgggttttca tttttgtcc 1140

104

ctttccccta gatccagaaa taaagtctaa gagaagcgca aaaaaaaaaa aaaaaaaaaa 1200
 aaaaaaaaaa aaaaaa 1215

<210> 327
 <211> 220
 <212> PRT
 <213> Homo sapien

<400> 327
 Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
 1 5 10 15
 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
 20 25 30
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
 35 40 45
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
 50 55 60
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
 65 70 75 80
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
 180 185 190
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
 195 200 205
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 328
 cgctcgctc tggtagctgc agccaaatca taaacggcga ggactgcagc ccgcactcgc 60
 agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc gtcctgggtgc 120
 atccgcagtg ggtgctgtca gccacacact gtttcagaa ctcctacacc atcgggctgg 180
 gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag gcca 234

<210> 329
 <211> 77
 <212> PRT
 <213> Homo sapien

<400> 329
 Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
 1 5 10 15
 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu

105

	20		25		30										
Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Ser	Ala	Thr
	35		40		45										
His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu
	50		55		60										
Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val	Glu	Ala			
65			70		75										

<210> 330
 <211> 70
 <212> DNA
 <213> Homo sapien

<400> 330
 cccaacacaa tggcccgatc ccatccctga ctccgccctc aggatcgctc gtctctggta 60
 gctgcagcca 70

<210> 331
 <211> 22
 <212> PRT
 <213> Homo sapien

	20		25		30										
Gln	His	Asn	Gly	Pro	Ile	Pro	Ser	Leu	Thr	Pro	Pro	Ser	Gly	Ser	Leu
	1		5		10									15	
Val	Ser	Gly	Ser	Cys	Ser										
			20												

<210> 332
 <211> 2507
 <212> DNA
 <213> Homo sapien

<400> 332
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 tgcccttcct tctgtatatg gctgcgcccc aaatcaggaa aatgctgtcc agtgggggtg 120
 gtacatcaac tgttcagctt cctgggaaag tagttgtggt cacaggagct aatacaggta 180
 tcgggaagga gacagccaaa gagctggctc agagaggagc tcgagtatat ttagcttgcc 240
 gggatgtgga aaagggggaa ttggtggcca aagagatcca gaccacgaca gggaaccagc 300
 aggtgttggg gcggaactg gacctgtctg atactaagtc tattcgagct tttgctaagg 360
 gcttcttagc tgaggaaaag cacctccacg ttttgatcaa caatgcagga gtgatgatgt 420
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 acttctcctt aacctatctg ctgctagaga aactaaagga atcagcccca tcaaggatag 540
 taaatgtgtc ttccctcgca catcacctgg gaaggatcca ctccataac ctgcagggag 600
 agaaattcta caatgcaggc ctggcctact gtcacagcaa gctagccaac atcctcttca 660
 cccaggaact ggcccggaga ctaaaaggct ctggcggttac gacgtattct gtacaccctg 720
 gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg tgggtggcttt 780
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 agattcgtct aaatgtctgt catgtccaga tttactttgc ttctgttact gccagagtta 1200
 ctagagatat cataatagga taagaagacc ctcatatgac ctgcacagct catttccctt 1260
 ctgaaagaaa ctactaccta ggagaatcta agctatagca gggatgattt atgcaaattt 1320
 gaactagctt ctttgttcac aattcagttc ctcccaacca accagtcttc acttcaagag 1380
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106

cccaggcatg	gtggatcacc	ggagggtcagt	agttcaagac	cagcctggcc	aacatggtga	1500
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agggagtatt	ttcacaaagt	tcaaaacagc	cacaataatc	agagatggag	caaaccagtg	1620
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tggaagataa	tgacaaaaat	gaagggacta	gttaaggatt	aactagccct	ttaaggatta	1800
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cttttattgc	acttgttttg	accattaagc	tatatgttta	gaaatgggtc	ttttacggaa	2340
aaattagaaa	aattctgata	atagtgcaga	ataaatgaat	taatgtttta	cttaatttat	2400
attgaactgt	caatgacaaa	taaaaattct	ttttgattat	tttttgtttt	catttaccag	2460
aataaaaacy	taagaattaa	aagtttgatt	acaaaaaaa	aaaaaaa		2507

<210> 333

<211> 3030

<212> DNA

<213> Homo sapien

<400> 333

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gctccatgga	gccccgcaat	tatgccagct	tggatggagc	caaggatata	gaaggcttgc	180
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cgctacgct	gatgcctgct	gtcaactatg	cccccttggg	tctgccaggc	tcggcggagc	300
cgccaaagca	atgccaccca	tgcctggggg	tgccccaggg	gacgtcccca	gctcccgtgc	360
cttatggtta	ctttggaggc	gggtactact	cctgcccagc	gtcccggagc	tcgctgaaac	420
cctgtgccca	ggcagccacc	ctggccgcgt	accccgcgga	gactcccacg	gccggggaag	480
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gacatgactc	cctgttgcc	gtggacagtt	accagtcttg	ggctctcgct	ggtggctgga	660
acagccagat	gtgttgccag	ggagaacaga	accaccagg	tcccttttgg	aaggcagcat	720
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aacgcattcc	gtacagcaag	gggcagttgc	gggagctgga	gcgggagtat	gcggctaaca	840
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<210> 334

<211> 2417

<212> DNA

<213> Homo sapien

<400> 334

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<210> 335

<211> 2984

<212> DNA

<213> Homo sapien

<400> 335

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<210> 336

<211> 147

<212> PRT

<213> Homo sapien

<400> 336

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20      25      30
Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
35      40      45
Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
50      55      60
Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
65      70      75      80
Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
85      90      95
Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
100     105     110
Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
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Ala Phe Trp
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<210> 337

<211> 9

<212> PRT

<213> Homo sapien

<400> 337

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<210> 338

<211> 9

<212> PRT

<213> Homo sapien

<400> 338

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<210> 339

<211> 318

<212> PRT

<213> Homo sapien

110

<400> 339

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Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly
 35          40          45
Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg
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Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu
 65          70          75          80
Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val
 85          90          95
Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys
 100         105         110
Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala
 115         120         125
Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met
 130         135         140
His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu
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 165         170         175
Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly
 180         185         190
Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala
 195         200         205
Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly
 210         215         220
Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val
 225         230         235         240
Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe
 245         250         255
Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu
 260         265         270
Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His
 275         280         285
Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg
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Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp
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<210> 340

<211> 483

<212> DNA

<213> Homo sapien

<400> 340

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111

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 <212> DNA
 <213> Homo sapien

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 <212> DNA
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<210> 344
 <211> 536
 <212> DNA
 <213> Homo sapien

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112

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<211> 251
<212> DNA
<213> Homo sapien

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<211> 282
<212> DNA
<213> Homo sapien

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<210> 347
<211> 201
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(201)
<223> n = A,T,C or G

<400> 347
acacacataa tattataaaa tgccatctaa ttggaaggag ctttctatca ttgcaagtca 60
taaataatac ttttaaaana ntactancag cttttaccta ngctcctaaa tgcttgtaaa 120
tctgagactg actggaccca cccagaccca gggcaaagat acatgttacc atatcatctt 180
tataaagaat ttttttttgt c 201

<210> 348
<211> 251
<212> DNA
<213> Homo sapien

<400> 348
ctgttaatca caacatttgt gcatcacttg tgccaagtga gaaaatgttc taaaatcaca 60
agagagaaca gtgccagaat gaaactgacc ctaagtccca ggtgccctg ggcaggcaga 120
aggagacact cccagcatgg aggagggtt atcttttcat cctaggtcag gtctacaatg 180
ggggaagggt ttattataga actcccaaca gccacactca ctctgccac ccaccgatg 240

113

gccctgcctc c 251

<210> 349
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 349

taaaaatcaa	gccattta	tgtatctttg	aaggtaaaca	atatatggga	gctggatcac	60
aacccctgag	gatgccagag	ctatgggtcc	agaacatggg	gtggatttat	caacagagtt	120
cagaagggtc	tgaactctac	gtgttaccag	agaacataat	gcaattcatg	cattccactt	180
agcaattttg	taaaatacca	gaaacagacc	ccaagagtct	ttcaagatga	ggaaaattca	240
actcctggtt	t					251

<210> 350
 <211> 908
 <212> DNA
 <213> Homo sapien

<400> 350

ctggacactt	tgcgagggtt	tttgcctggt	gctgctgctg	cccgatcatg	tactcatcgt	60
agcccgcccg	gtgaagctcg	ctgctttccc	tacctcctta	agtgactgcc	aaacgcccac	120
cggttggaat	tgctctggtt	atgatgacag	agaaaatgat	ctcttcctct	gtgacaccaa	180
cacctgtaaa	tttgcctggg	aattgtttaag	aattggagac	actgtgactt	gcgtctgtca	240
gttcaagtgc	aacaatgact	atgtgcctgt	gtgtggctcc	aatggggaga	gctaccagaa	300
tgagtgttac	ctgcgacagg	ctgcatgcaa	acagcagagt	gagatacttg	tggtgtcaga	360
aggatcatgt	gccacagtcc	atgaagggtc	tgagagaaact	agtcaaaaagg	agacatccac	420
ctgtgatatt	tgccagtttg	gtgcagaatg	tgacgaagat	gccgaggatg	tctggtgtgt	480
gtgtaataat	gactgttctc	aaaccaactt	caatcccctc	tgcgcttctg	atgggaaatc	540
ttatgataat	gcatgccaaa	tcaaagaagc	atcgtgtcag	aaacaggaga	aaattgaagt	600
catgtctttg	ggctgatgtc	aagataacac	aactacaact	actaagtctg	aagatgggca	660
ttatgcaaga	acagattatg	cagagaatgc	taacaaatta	gaagaaaagt	ccagagaaca	720
ccacatacct	tgtccggaac	attacaatgg	cttctgcgat	catgggaagt	gtgagcattc	780
tatcaatgat	caggagccat	cttgcagggt	tgatgctggg	tatactggac	aacactgtga	840
aaaaaaggac	tacagtgttc	tatacgttgt	tcccggctct	gtacgatttc	agtatgtcct	900
aatcgcatg						908

<210> 351
 <211> 472
 <212> DNA
 <213> Homo sapien

<400> 351

ccagttattt	gcaagtggta	agagcctatt	taccataaat	aatactaaga	accaactcaa	60
gtcaaacctt	aatgpcattg	ttattgtgaa	ttaggattaa	gtagtaattt	tcaaaattca	120
cattaacttg	attttaaaa	cagwtttgyg	agtcattttac	cacaagctaa	atgtgtacac	180
tatgataaaa	acaaccattg	tattcctgtt	tttctaaaca	gtcctaattt	ctaactctgt	240
atatatcctt	cgacatcaat	gaactttgtt	ttcttttact	ccagtaataa	agtaggcaca	300
gatctgtcca	caacaaactt	gccctctcat	gccttgccctc	tcaccatgct	ctgctccagg	360
tcagccccc	tttggcctgt	ttgttttgtc	aaaaacctaa	tctgcttctt	gcttttcttg	420
gtaatatata	tttagggaag	atgttgcttt	gccacacac	gaagcaaagt	aa	472

<210> 352
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 352

114

ctcaaagcta	atctctcggg	aatcaaacca	gaaaagggca	aggatcttag	gcatgggtgga	60
tgtggataag	gccaggtcaa	tggtctgcaag	catgcagaga	aagaggtaca	tcggagcgtg	120
caggctgcgt	tccgtcctta	cgatgaagac	cacgatgcag	tttccaaaca	ttgccactac	180
atacatggaa	aggaggggga	agccaaccca	gaaatgggct	ttctctaata	ctgggatacc	240
aataagcaca	a					251

<210> 353
 <211> 436
 <212> DNA
 <213> Homo sapien

<400> 353						
tttttttttt	tttttttttt	ttttttacaa	caatgcagtc	atatttttat	tgagtatgtg	60
cacattatgg	tattattact	atactgatta	tatttatcat	gtgacttcta	attaraaaat	120
gtatccaaaa	gcaaaacagc	agatatacaa	aattaaagag	acagaagata	gacattaaca	180
gataaggcaa	cttatacatt	gacaatccaa	atccaataca	tttaaactat	tgggaaatga	240
gggggacaaa	tggaagccar	atcaaatttg	tgtaaaacta	ttcagtatgt	ttcccttgct	300
tcatgtctga	raaggctctc	ccttcaatgg	ggatgacaaa	ctocaaatgc	cacacaaatg	360
ttaacagaat	actagattca	cactggaacg	ggggtaaaga	agaaattatt	ttctataaaa	420
gggtctctaa	tgtagt					436

<210> 354
 <211> 854
 <212> DNA
 <213> Homo sapien

<400> 354						
ccttttctag	ttcaccagtt	ttctgcaagg	atgctgggta	gggagtgtct	gcaggaggag	60
caagtctgaa	accaaactca	ggaaacatag	gaaacgagcc	aggcacaggg	ctggtgggccc	120
atcaggggacc	accctttggg	ttgatatttt	gcttaactctg	catcttttga	gtaagatcat	180
ctggcagtag	aagctgttct	ccagggtacat	ttctctagct	catgtacaaa	aacatcctga	240
aggactttgt	caggtgcctt	gctaaaagcc	agatgcgttc	ggcacttcct	tggtctgagg	300
ttaattgcac	acctacaggc	actgggctca	tgctttcaag	tattttgtcc	tcactttagg	360
gtgagtgaag	gatccccatt	ataggagcac	ttgggagaga	tcataataaa	gctgactctt	420
gagtacatgc	agtaatgggg	tagatgtgtg	tggtgtgtct	tcatttcctgc	aagggtgctt	480
gttagggagt	gtttccagga	ggaacaagtc	tgaaaccaat	catgaaataa	atggtaggtg	540
tgaactggaa	aactaattca	aaagagagat	cgtgatatca	gtgtgggtga	tacaccttgg	600
caatatggaa	ggctctaatt	tgcccatatt	tgaaataata	attcagcttt	ttgtaataca	660
aaataacaaa	ggatttgaaa	tcatgggtgc	taatgtataa	aagaccagag	aaacataaat	720
atatcaactg	cataaatgta	aaatgcatgt	gaccaagaa	ggccccaag	tggcagacaa	780
cattgtaccc	attttccctt	ccaaaatgtg	agcggcgggc	ctgctgcttt	caaggctgtc	840
acacgggatg	tcag					854

<210> 355
 <211> 676
 <212> DNA
 <213> Homo sapien

<400> 355						
gaaattaagt	atgagctaaa	ttccctgtta	aaacctctag	gggtgacaga	tctcttcaac	60
cagggtcaaa	ctgacttttc	tggaatgtca	ccaaccaagg	gcctatatth	atcaaaagcc	120
atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
gacagcatcg	ctgtaaaaag	cctaccaatg	agagctcagt	tcaaggcgaa	ccacccttcc	240
ctgtttctta	taaggcacac	tcataccaac	acgatccctat	tctgtggcaa	gcttgccctc	300
ccctaatacag	atgggggttg	gtaaggctca	gagttgcaga	tgagggtgcag	agacaatcct	360
gtgactttcc	cacggccaaa	aaagctgttc	cacctcacgc	acctctgtgc	ctcagtttgc	420
tcactctgaa	aatagggtota	ggattttctc	caaccatttc	atgagttgtg	aagctaaggc	480
tttggttaatc	atggaaaaag	gtagacttat	gcagaaagcc	tttctggctt	tcttatctgt	540

115

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ggtgtctcat ttgagtgtg tccagtgaca tgatcaagtc aatgagtaaa attttaaggg    600
attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgacc tgacatctct    660
gcttaaagaa aaccag                                     676

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<210> 356
<211> 574
<212> DNA
<213> Homo sapien

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<400> 356
tttttttttt tttttcagga aaacattctc ttactttatt tgcattctcag caaaggttct    60
catgtggcac ctgactggca tcaaaccaaa gtctgtaggc caacaaagat gggccactca    120
caagcttccc attttagat ctgagtgcct atgagtatct gacacctgtt cctctcttca    180
gtctcttagg gaggcttaaa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc    240
aaaagtccac aaaactgcag tctttgctgg gatagtaagc caagcagtcg ctggacagca    300
gagttctttt cttgggcaac agataaccag acaggactct aatcgtgctc ttattcaaca    360
ttcttctgtc tctgcctaga ctggaataaa aagccaatct ctctcgtggc acaggggaag    420
agatacaagc tcgtttacat gtgatagatc taacaaaggc atctaccgaa gtctggtctg    480
gatagacggc acagggagct cttaggtcag cgctgctggg tggaggacat tcctgagtc    540
agctttgcag cctttgtgca acagtacttt ccca                                     574

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<210> 357
<211> 393
<212> DNA
<213> Homo sapien

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<400> 357
tttttttttt tttttttttt tttttttttt tacagaatat aratgcttta tcactgkact    60
taatatggkg kcttyttcac tatacttaaa aatgcaccac tcataaatat ttaattcagc    120
aagccacaac caaracttga ttttatcaac aaaaaccctt aaatataaac ggsaaaaaag    180
atagatataa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara    240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa    300
gcataatctg taaaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct    360
tttttttctt tttctgtttt tttttttttt tac                                     393

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<210> 358
<211> 630
<212> DNA
<213> Homo sapien

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<400> 358
acagggtaaa caggaggatc cttgctctca cggagcttac attctagcag gaggacaata    60
ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga    120
gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taagggaagtg    180
gagtttaaac tgagagaagc aagtgcctaa actgaaggat gtgttgaaga agaagggaga    240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaagggt tcaaagaact    300
gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag    360
attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa    420
tcactgaagg gagtaatgtg acattacttt tcaattcagg atggccattc taactccagg    480
gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcgatagt    540
gaaagacaaa aataagtggg gaaattcagg ggatagtga aatcagtagg acttaatgag    600
caagccagag gttcctccac aacaaccagt                                     630

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<210> 359
<211> 620
<212> DNA
<213> Homo sapien

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116

<400> 359

acagcattcc	aaaatataca	tctagagact	aarrgtaaat	gctctatagt	gaagaagtaa	60
taattaaana	atgctactaa	tatagaaaat	ttataatcag	aaaaataaat	attcagggag	120
ctcaccagaa	gaataaagt	ctctgccagt	tattaaagga	ttactgctgg	tgaattaaat	180
atggcattcc	ccaagggaaa	tagagagatt	cttctggatt	atgttcaata	tttatttcac	240
aggattaact	gttttaggaa	cagatataaa	gcttcgccac	ggaagagatg	gacaaagcac	300
aaagacaaca	tgataacctta	ggaagcaaca	ctaccctttc	aggcataaaa	tttggagaaa	360
tgcaacatta	tgcttcatga	ataatatgta	gaaagaaggt	ctgatgaaaa	tgacatcctt	420
aatgtaagat	aactttataa	gaattctggg	tcaaataaaa	ttctttgaag	aaaacatcca	480
aatgtcattg	acttatcaaa	tactatcttg	gcataatacc	tatgaaggca	aaactaaaca	540
aacaaaaagc	tcacaccaaa	caaaaccatc	aacttatatt	gtattctata	acatacgaga	600
ctgtaaagat	gtgacagtgt					620

<210> 360

<211> 431

<212> DNA

<213> Homo sapien

<400> 360

aaaaaaaaa	agccagaaca	acatgtgata	gataatatga	ttggctgcac	acttccagac	60
tgatgaatga	tgaacgtgat	ggactattgt	atggagcaca	tcttcagcaa	gagggggaaa	120
tactcatcat	ttttggccag	cagttgtttg	atcaccaaaac	atcatgccag	aatactcagc	180
aaaccttctt	agctcttgag	aagtcaaagt	ccgggggaat	ttattcctgg	caattttaat	240
tggactcctt	atgtgagagc	agcggctacc	cagctggggg	ggtggagcga	acccgtcact	300
agtggacatg	cagtggcaga	gctcctggta	accacctaga	ggaatacaca	ggcacatgtg	360
tgatgccaag	cgtgacacct	gtagcactca	aatttgtctt	gtttttgtct	ttcgggtgtgt	420
agattcttag	t					431

<210> 361

<211> 351

<212> DNA

<213> Homo sapien

<400> 361

acactgattt	ccgatcaaaa	gaatcatcat	otttaccttg	acttttcag	gaattactga	60
actttcttct	cagaagatag	ggcacagcca	ttgccttggc	ctcacttgaa	gggtctgcat	120
ttgggtctct	tggtctcttg	ccaagtttcc	cagccactcg	agggagaaat	atcgggaggt	180
ttgacttctt	ccggggcttt	cccgagggct	tcacctgtag	ccctgcggcc	ctcagggctg	240
caatcctgga	ttcaatgtct	gaaacctcgc	tctctgcctg	ctggacttct	gaggccgtca	300
ctgccactct	gtcctccagc	tctgacagct	cctcatctgt	ggtcctgttg	t	351

<210> 362

<211> 463

<212> DNA

<213> Homo sapien

<400> 362

acttcatcag	gccataatgg	gtgcctcccg	tgagaatcca	agcacctttg	gactgcgcga	60
tgtagatgag	ccggtggaag	atcttgcgca	tgccgggctt	cagggcgaa	ttcttggcgc	120
ccccggtcac	agaaatgacc	aggttgggtg	ttttcaggtg	ccagtgtctg	gtcagcagct	180
cgtaaaggat	ttccgcgtcc	gtgtcgcagg	acagacgtat	atacttccct	ttcttcccca	240
gtgtctcaaa	ctgaatatcc	ccaaaggcgt	cggtaggaaa	ttccttgggtg	tgtttcttgt	300
agttccattt	ctcacttttg	ttgatctggg	tgcttcccat	gtgctggctc	tgggcatagc	360
cacacttgca	cacattctcc	ctgataagca	cgatgggtgtg	gacaggaagg	aaggatttca	420
ttgagcctgc	ttatggaaac	tggatttgtt	agcttaataa	gac		463

<210> 363

<211> 653

117

<212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(653)
 <223> n = A,T,C or G

<400> 363
 acccccaggt ncctgncctgg catactgnga acgaccaacg acacacccaa gctcggcctc 60
 ctcttgngga ttctgggtga catcttcattg aatggcaacc gtgccagwga ggctgtcctc 120
 tgggaggcac tacgcaagat gggactgcgt cctgggggtga gacatcctct ccttgagat 180
 ctaacgaaac ttctcaccta tgagtgttaa agcagaaata cctgnactac agacgagtgc 240
 ccaacagcaa cccccggaa gtatgagttc ctctrgggcc tccgttccta ccatgagasc 300
 tagcaagatg naagtgttga gantcattgc agaggttcag aaaagagacc cntcgtgact 360
 ggtctgcaca gttcatggag gctgcagatg aggccttgga tgctctggat gctgctgcag 420
 ctgaggccga agcccgggct gaagcaagaa cccgcatggg aattggagat gaggctgtgt 480
 ntgggccctg gagctgggat gacattgagt ttgagctgct gacctgggat gaggaaggag 540
 attttgagaga tccntgggtcc agaattccat ttaccttctg ggccagatac caccagaatg 600
 cccgctccag attccctcag acctttgccg gtcccattat tggctcstggt ggt 653

<210> 364
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 364
 actagaggaa agacgttaaa ccactctact accacttgtg gaactctcaa agggtaaattg 60
 acaaagccaa tgaatgactc taaaaacaat atttacattt aatgggtttgt agacaataaa 120
 aaaacaaggt ggatagatct agaattgtaa cattttaaga aaaccatagc atttgacaga 180
 tgagaaagct caattataga tgcaaagtta taactaaact actatagtag taaagaaata 240
 catttcacac ccttcatata aattcactat cttggcttga ggcaactccat aaaatgtatc 300
 acgtgcatag taaatcttta tatttgctat ggcgttgcaac tagaggactt ggactgcaac 360
 aagtggatgc gcggaaaatg aaatcttctt caatagccca g 401

<210> 365
 <211> 356
 <212> DNA
 <213> Homo sapien

<400> 365
 ccagtgtcat atttgggctt aaaatttcaa gaagggcact tcaaattggct ttgcatttgc 60
 atgtttcagt gctagagcgt aggaatagac cctggcgctc actgtgagat gttcttcagc 120
 taccagagca tcaagtctct gcagcaggtc attcttgggt aaagaaatga cttccacaaa 180
 ctctccatcc cctggctttg gcttcggcct tgcgttttcg gcatcatctc cgtaaatggt 240
 gactgtcacg atgtgtatag tacagtttga caagcctggg tccatacaga ccgctggaga 300
 acattcggca atgtcccctt tgtagccagt ttcttcttcg agctcccgga gagcag 356

<210> 366
 <211> 1851
 <212> DNA
 <213> Homo sapien

<400> 366
 tcatcaccat tgccagcagc ggcaccgtta gtcaggtttt ctgggaatcc cacatgagta 60
 cttccgtgtt cttcattctt cttcaatagc cataaatctt ctagctctgy ctggctgttt 120
 tcaattcctt taagcctttg tgactcttcc tctgatgtca gctttaagtc ttgttctgga 180
 ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg 240

118

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caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag 300
aagatacatc aacatthttgc tcaagtagag ggctgactat acttgctgat ccacaacata 360
cagcaagtat gagagcagtt cttccatata tatccagcgc atttaaattc gcttttttct 420
tgattaaaaa tttcaccact tgctgttttt gctcatgtat accaagtagc agtggtgtga 480
ggccatgctt gttttttgat tcgatatcag caccgtataa gagcagtgc tggccatta 540
atttatcttc attgtagaca gcatagtgtg gagtggtatt tccatactca tctggaatat 600
ttgcatcagt gccatgttcc agcaacatta acgcacattc atcttcctgg cattgtacgg 660
cctttgtcag agctgtcctc tttttgttgt caaggacatt aagttgacat cgtctgtcca 720
gcacgagttt tactacttct gaattcccat tggcagaggc cagatgtaga gcagtcctct 780
tttgcttgtc cctcttggtc acatccgtgt ccctgagcat gacgatgaga tcctttctgg 840
ggactttacc ccaccaggca gctctgtgga gcttgtccag atcttctcca tggacgtggt 900
acctgggatac catgaaggcg ctgtcatcgt agtctcccca agcgaccacg ttgctcttgc 960
cgtccctctg cagcagggga agcagtgcca gcaccacttg cactcttgc tcccaagcgt 1020
cttcacagag gagtcgttgt ggtctccaga agtgcccacg ttgctcttgc cgtcccccct 1080
gtccatccag ggaggaagaa atgcaggaaa tgaaagatgc atgcacgatg gtatactcct 1140
cagccatcaa acttctggac agcaggtcac ttccagcaag gtggagaaaag ctgtccaccc 1200
acagaggatg agatccagaa accacaatat ccattcacaa acaaactt ttcagccaga 1260
cacaggtaact gaaatcatgt catctgcggc aacatggtgg aacctacca atcacacatc 1320
aagagatgaa gacactgcag tatactctgca caacgtaata ctcttcatcc ataacaaaat 1380
aatataattt tctcttgag ccatatggat gaactatgaa ggaagaactc cccgaagaag 1440
ccagtgcgag agaagccaca ctgaagctct gtcctcagcc atcagcgcca cggacagggar 1500
tgtgtttctt cccagtgat gcagcctcaa gttatcccga agctgccgca gcacacgggtg 1560
gtctctgaga aacacccag ctctccgt ctaacacagg caagtcaata aatgtgataa 1620
tcacataaac agaattaaaa gcaaagtcac ataagcatct caacagacac agaaaaggca 1680
tttgacaaaa tccagcatcc ttgtatttat tgttgagtt ctcagaggaa atgcttctaa 1740
ctttcccca ttttagtatta tgttggtgt gggcttgtca tagtggtgtt ttattacttt 1800
aaggtatgtc ccttctatgc ctgttttgc gagggtttta attctcgtgc c 1851

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<210> 367
 <211> 668
 <212> DNA
 <213> Homo sapien

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<400> 367
cttgagcttc caaataygga agactggccc ttacacasgt caatgttaaa atgaatgcat 60
ttcagtattht tgaagataaa attrgtagat ctataccttg ttttttgatt cgatatcagc 120
acctataaag agcagtgcct tggccattaa tttatcttcc attrtagaca gcrtagtgya 180
gagtggtatt tccatactca tctggaatat ttggatcagt gccatgttcc agcaacatta 240
acgcacattc atcttcctgg cattgtacgg cctgtcagta ttagacccaa aaacaaatta 300
catatcttag gaattcaaaa taacattcca cagcttccac caactagtta tatttaaagg 360
agaaaactca tttttatgcc atgtattgaa atcaaaccce cctcatgctg atatagtthg 420
ctactgcata cctttatcag agctgtcctc tttttgttgt caaggacatt aagttgacat 480
cgtctgtcca gcaggagttt tactacttct gaattcccat tggcagaggc cagatgtaga 540
gcagtcctat gagagtgaga agacttttta ggaaattgta gtgcactagc tacagccata 600
gcaatgattc atgtaactgc aaacactgaa tagcctgcta ttactctgcc ttcaaaaaaa 660
aaaaaaa

```

<210> 368
 <211> 1512
 <212> DNA
 <213> Homo sapien

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<400> 368
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<210> 369

<211> 1853

<212> DNA

<213> Homo sapien

<400> 369

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120

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<210> 370
 <211> 2184
 <212> DNA
 <213> Homo sapien

<400> 370

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<210> 371
 <211> 1855
 <212> DNA
 <213> Homo sapien

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<400> 371

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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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<210> 373

<211> 1155

122

<212> DNA

<213> Homo sapien

<400> 373

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<210> 374

<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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123

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<210> 375

<211> 2040

<212> DNA

<213> Homo sapien

<400> 375

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tgtgtgctgc	actgtctccc	ctgctgcagg	gggagcggca	agagcaaggt	gggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccaggtacc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctggtggggg	aaagtcacca	gaaaggatct	catcgtcatg	480
ctcaggggaca	ctgacgtgaa	caagaaggac	aagcaaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcc	ggaagatgaa	660
tgtgcgttaa	tgttgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatacgaatc	aaaaaacaag	catggcctca	caccactgtt	acttgggtgta	840
catgagcaaa	aacagcaagt	cgtgaaattt	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgctgtat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggaacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaca	agacttaaa	1140
ctgacatcag	aggaagagtc	acaaagggtc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	aggttgaaga	agaaatgaag	1260
aagcatgaaa	gtaataatgt	gggattacta	gaaaacctga	ctaattggtg	cactgctggc	1320
aatggtgata	atggattaat	tcctcaaagg	aagagcagaa	cacctgaaaa	tcagcaattt	1380
cctgacaacg	aaagtgaaga	gtatcacaga	atttgcgaat	tagtttctga	ctacaaaaga	1440
aaacagatgc	caaaaacttc	ttctgaaaac	agcaacccag	aacaagactt	aaagctgaca	1500
tcagaggaag	agtcacaaag	gcttgagggc	agtgaaaatg	gccagccaga	gaaaagatct	1560
caagaaccag	aaataaataa	ggatgggtgat	agagagctag	aaaattttat	ggctatcgaa	1620
gaaatgaaga	agcacggaag	tactcatgtc	ggattcccag	aaaacctgac	taatggtgcc	1680
actgctggca	atggtgatga	tggattaatt	cctccaagga	agagcagaac	acctgaaagc	1740
cagcaatttc	ctgacactga	gaatgaagag	tatcacagtg	acgaacaaaa	tgatactcag	1800
aagcaatttt	gtgaagaaca	gaacactgga	atattacacg	atgagattct	gattcatgaa	1860
gaaaagcaga	tagaagtggt	tgaaaaaatg	aattctgagc	tttctcttag	ttgtaagaaa	1920
gaaaagagaca	tcttgcata	aaatagtagc	ttgcgggaag	aaattgccat	gctaagactg	1980
gagctagaca	caatgaaaca	tcagagccag	ctaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2040

<210> 376

<211> 329

<212> PRT

<213> Homo sapien

<400> 376

Met	Asp	Ile	Val	Val	Ser	Gly	Ser	His	Pro	Leu	Trp	Val	Asp	Ser	Phe
1				5					10					15	
Leu	His	Leu	Ala	Gly	Ser	Asp	Leu	Leu	Ser	Arg	Ser	Leu	Met	Ala	Glu

124

```

      20      25      30
Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
      35      40      45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
      50      55      60
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
      65      70      75      80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
      85      90      95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
      100      105      110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
      115      120      125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
      130      135      140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
      145      150      155      160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
      165      170      175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
      180      185      190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
      195      200      205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
      210      215      220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
      225      230      235      240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
      245      250      255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
      260      265      270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
      275      280      285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
      290      295      300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
      305      310      315      320
Ser Met Leu Phe Leu Val Ile Ile Met
      325

```

<210> 377

<211> 148

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1)...(148)

<223> Xaa = Any Amino Acid

<400> 377

```

Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
  1      5      10      15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
      20      25      30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
      35      40      45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu

```

125

```

      50              55              60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65              70              75              80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
      85              90              95
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
      100              105              110
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
      115              120              125
Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
      130              135              140
Lys Asn Lys Val
145

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<210> 378
<211> 1719
<212> PRT
<213> Homo sapien

```

```

      <400> 378
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1              5              10              15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20              25              30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35              40              45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
      50              55              60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65              70              75              80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85              90              95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100              105              110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115              120              125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
      130              135              140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145              150              155              160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
      165              170              175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
      180              185              190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
      195              200              205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
      210              215              220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225              230              235              240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
      245              250              255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
      260              265              270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
      275              280              285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
290              295              300

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126

Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355				360					365				
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys
	370				375						380				
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser
385					390					395					400
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys
				405					410					415	
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly
			420					425					430		
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys
		435					440					445			
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly
	450					455				460					
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys
465					470					475					480
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys
			485						490					495	
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp
			500					505					510		
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu
	515						520					525			
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp
	530					535					540				
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln
545					550					555					560
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val
				565					570					575	
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn
			580					585					590		
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu
		595				600						605			
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp
	610					615					620				
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys
625					630					635					640
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys
				645					650					655	
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys
			660					665					670		
Gln	Gln	Val	Val	Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala
		675					680					685			
Leu	Asp	Arg	Tyr	Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly
	690					695					700				
Ser	Ala	Ser	Ile	Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser
705					710					715					720
Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser
				725					730					735	
His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln
			740					745					750		
Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys
		755					760						765		

127

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Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser
  770          775          780
Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp
  785          790          795          800
Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly
          805          810          815
Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn
          820          825          830
Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe
  835          840          845
Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser
  850          855          860
Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn
  865          870          875          880
Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu
          885          890          895
Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile
  900          905          910
Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn
  915          920          925
Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro
  930          935          940
Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu
  945          950          955          960
Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe
          965          970          975
Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His
  980          985          990
Glu Glu Lys Gln1 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser
  995          1000          1005
Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu
  1010          1015          1020
Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His
  1025          1030          1035          1040
Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met
          1045          1050          1055
Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met
          1060          1065          1070
Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys
  1075          1080          1085
Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr
  1090          1095          1100
Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys
  1105          1110          1115          1120
Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp
          1125          1130          1135
Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His
          1140          1145          1150
Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp
  1155          1160          1165
Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg
  1170          1175          1180
Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val
  1185          1190          1195          1200
Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys
          1205          1210          1215
Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly
          1220          1225          1230

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128

Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn
 1235 1240 1245
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys
 1250 1255 1260
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro
 1265 1270 1275 1280
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr
 1285 1290 1295
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp
 1300 1305 1310
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val
 1315 1320 1325
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala
 1330 1335 1340
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala
 1345 1350 1355 1360
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn
 1365 1370 1375
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr
 1380 1385 1390
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr
 1395 1400 1405
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu
 1410 1415 1420
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly
 1425 1430 1435 1440
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn
 1445 1450 1455
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser
 1460 1465 1470
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly
 1475 1480 1485
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu
 1490 1495 1500
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys
 1505 1510 1515 1520
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser
 1525 1530 1535
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu
 1540 1545 1550
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser
 1555 1560 1565
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe
 1570 1575 1580
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe
 1585 1590 1595 1600
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly
 1605 1610 1615
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro
 1620 1625 1630
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln
 1635 1640 1645
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile
 1650 1655 1660
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser
 1665 1670 1675 1680
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn
 1685 1690 1695

129

Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr
 1700 1705 1710
 Met Lys His Gln Ser Gln Leu
 1715

<210> 379
 <211> 656
 <212> PRT
 <213> Homo sapien

<400> 379
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu

130

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      370      375      380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385      390      395      400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
      405      410      415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
      420      425      430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
      435      440      445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
      450      455      460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465      470      475      480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
      485      490      495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
      500      505      510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
      515      520      525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
      530      535      540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545      550      555      560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
      565      570      575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
      580      585      590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
      595      600      605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
      610      615      620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625      630      635      640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
      645      650      655

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<210> 380

<211> 671

<212> PRT

<213> Homo sapien

<400> 380

```

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1      5      10      15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20      25      30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35      40      45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
      50      55      60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65      70      75      80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85      90      95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100      105      110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115      120      125

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131

Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
130						135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180					185					190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
	195						200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
210						215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245					250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
			275				280					285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
290						295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355				360						365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
		370				375					380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395					400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
			420					425				430			
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
		435					440					445			
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
		450				455					460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470					475					480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485					490					495	
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
			500					505					510		
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp
		515					520					525			
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys
530						535					540				
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala
545					550					555					560
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg
				565					570					575	
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His
			580					585						590	

132

Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
 595 600 605
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
 610 615 620
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys
 625 630 635 640
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala
 645 650 655
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 660 665 670

<210> 381
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 381
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa 60
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcacatgac ctctgagggg 120
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggacca ggactcacac 180
 atcctggggc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa 240
 caagcagtcg g 251

<210> 382
 <211> 3279
 <212> DNA
 <213> Homo sapiens

<400> 382
 cttcctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtggt 120
 cactgggagg ggacatcctg cagaaggtag gagtgcagaa acacccgctg caggggaggg 180
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggagggag 240
 gggcctggag ggcgtgagga ggagcaggg ggctgcatgg ctggagttag ggatcagggg 300
 cagggcgcgga gatggcctca cacaggggaag agagggcccc tctgcaggg cctcacctgg 360
 gccacaggag gacactgctt ttcctctgag gagtgcaggag ctgtggatgg tgctggacag 420
 aagaaggaca gggcctggct cagggtgtcca gaggtgtcgt ctggcttccc tttgggatca 480
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
 gtggctccag gcctgcccc tgctggggc ctacccagc ctccctcaca gtctcctggc 600
 cctcagttct tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatact 660
 gaactgacca taccagccc tgcccacggc cctccatggc tccccaatgc cctggagagg 720
 ggacatctag tcagagagta gtctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
 gcacctctga gatggtcccg gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840
 ggaccttgcc ccttggtgcag gagctggacc ctgaagtccc ctccccatag gccaagactg 900
 gagccttggt ccctctgttg gactocctgc ccatattctt gtgggagtggt gttctggaga 960
 catttctgtc tgttctctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020
 agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggatatcac 1140
 atcatggggc cctgagccat gtgccctgcc tgaagagcct gctgtgtaca ccaagtggtt 1200
 gcattaccgg aagtgagatca aggacacat cgcagccaac cctgagtgcc ccctgtccca 1260
 cccctacctc tagtaaatat aagtccacct cacgttctgg catcacttgg cctttctgga 1320
 tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gagtccact 1380
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 tgtttgtggg gttcagagat gggaggggtg gggccacccc tggaagagt gacagtga 1620
 caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680
 acacacagca aggttgacgc tgtaaacata gccacgctg tctggggggc actgggaagc 1740

```

ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttggtg aaggagggac 1800
tagggggaga aactgaaagc tgattaatta caggagggtt gttcagggtc cccaaaccac 1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaacaa aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040
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gtagctgatac cagctgatag aggaactagc cagggtgggg cctttccctt tggatggggg 2160
gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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tgaagtcctc agacctgagg ttccctagag ttcaaacaga tacagcatgg tccagagtcc 2400
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aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760
atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca cccacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940
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acaagacggt ggggcaagact ctgatttccg tgggggaatg tcatgggtctt gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccagggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

```

<210> 383

<211> 154

<212> PRT

<213> Homo sapiens

<400> 383

```

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5              10              15
Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20              25              30
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35              40              45
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50              55              60
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65              70              75              80
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85              90              95
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100             105             110
Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115             120             125
Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130             135             140
Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145             150

```

<210> 384

<211> 557

<212> DNA

<213> Homo sapiens

134

```

<400> 384
ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
aaagatgtgt tttgttttg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaagggt cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggg 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat ccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540
aaaaaaaaaa aaaaaaa 557

```

```

<210> 385
<211> 337
<212> DNA
<213> Homo sapiens

```

```

<400> 385
ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
ttcacaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
aaaagctggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattccccc ttttcacat cccgga 337

```

```

<210> 386
<211> 300
<212> DNA
<213> Homo sapiens

```

```

<400> 386
gggcccgtc cccgcccagg cccgcctcg cgagtccctc tcccgggtg cctgcccga 60
gcccgctcg cccagagggt gggcggggg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttg cccgaaggct ctgcaagga cccaccgacc ccagccgagg cggcgggcgc 180
gcggactttg cccggtgtgt gggcgggagc ggactgcgtg tccgaggacg ggcagcgaag 240
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

```

```

<210> 387
<211> 537
<212> DNA
<213> Homo sapiens

```

```

<400> 387
gggcagagtc gggcaccaag ggaactcttg caggcttctt tcctcggatc atcaaggctg 60
cccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggtctctg ggcggctgaa aggggcaagg aggcaaggac ccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttctc agcactgagg 240
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
gcggcccagc acttcctcag acacaacttc ttctgtctgc tccagtctg gggatcatca 360
cttaaccacc cccaagtgc aagaccaaat cttccagctg ccccttctg gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctacagcctg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaa 537

```

```

<210> 388
<211> 520
<212> DNA
<213> Homo sapiens

```

135

```

<400> 388
aggataatTTT ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggTTTaaa ccagTTtgca ttccctaata gtggaaaaag taaggaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatctcactt gccaaagtga 180
ggacccccctc cccaacatgc ccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttTtg gacctcacca gagaccagga gggTTtggt agctcacagg 300
acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360
tcatactcaa ttgatggTta ttagacaatt ccatttcttt ctggTTatta taaacagaaa 420
atctttctc tttctattac cagtaaaggc tcttggtatc tttctgttg aatgatttct 480
atgaacttgt cttattttaa tggTgggtt ttttctggt 520

```

```

<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

```

```

<400> 389
cgttgcccca gtttgacaga aggaaggcg gagcttattc aaagtctaga gggagtggag 60
gagTTaaggc tggatttcag atctgcctgg ttccagccgc agtTgcccct ctgctcccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcaccgc ctgtctcac agctgagact 240
cccaggaaac cttcagacta ctttctctg cttcagcaa ggggcgttg ccacattctc 300
tgagggtcag tggaagaacc tagactcca ttgctagagg tagaaaggg aagggtgctg 360
gggag 365

```

```

<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

```

```

<400> 390
tgctctcca tcttgcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacgntt ctcatgggtg tggaaatct ctgcttgagg ttccaggaag gcctctggt 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagTTaag gctgatttc a 221

```

```

<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

```

```

<400> 391
tggagcaggT cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccg ntaccagccc 240
cactgcccag gaatctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300

```


136

gagacctccg gctactacta tgacc

325

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(277)

<223> n = A,T,C or G

<400> 392

```

atattgttta actccttcct ttatatcttt taacattttc atggngaaag gttcacatct 60
agtctcactt nggcnagnn ctctacttg agtctcttcc cgggcctggn ccagtnгнаa 120
antaccanga accgncatgn cttanaacn ncctggttn tgggttnntc aatgactgca 180
tgacagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

```

<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

```

actagtccag tgtggtggaa ttgcgggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gaggtttcaa ccttagccca tctgcgggca 180
gagaaggctc agtttgtcca tcagcattat catgatatac ggactgggta cttgggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtgggttt caaaagtaga aatgtcctgt attccgatga tcacocgtga aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttggtt aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa 566

```

<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

```

gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tccaagatt atcgggagaa agggggcagt aattacccaa atccgggttg agcatgacgt 240
gaacatccag ttctctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384

```

<210> 395

<211> 399

<212> DNA

137

<213> Homo sapiens

<400> 395

```

ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttcagttacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac 399

```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```

tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctacacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctat 360
atcaaagcag gtgctatcac tcaatgtag gccctgctct ttt 403

```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

```

actagtnacg tgtggtggaa ttcgcggccg cgtcgaccta naanccatct ctatagcaaa 60
tccatccccg ctcttggttg gtnacagaat gactgacaaa 100

```

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398

```

gcggccgcgt cgacagcagt tccgccagcg ctgcgccctg ggtggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggttg actcatcatg 180

```

138

ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
 ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399

<211> 298

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(298)

<223> n = A,T,C or G

<400> 399

acggagggtg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
 ggggtgcnng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
 ccgagatcga gcgcatgggc ctggatcatgg accgcatggg ctccgtggag cgcgtgggct 180
 ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggccctccanc attgancgca 240
 tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcattggg 298

<210> 400

<211> 548

<212> DNA

<213> Homo sapiens

<400> 400

acatcaacta cttcctcatt ttaaggatg gcagttccct tcctccctt ttctgcctt 60
 gtacatgtac atgtatgaaa ttcccttctc ttaccgaact ctctccacac atcacaagggt 120
 caaagaacca cagccttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
 tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
 tgagagggc tagagaatta ttccatacag gctttgaggc caccatgtc acttatcccg 300
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
 gttggcccca taattctggg cctttgttgt ttgttttaac tacttgggca tcccaggaag 420
 ctttccagtg atctcctacc atgggcccc ctccctgggag caagccctc ccaggccctg 480
 tccccagccc ctctgcccc agcccaccgc cttgccttgg tgcctagccc tcccattggg 540
 agcagggtt 548

<210> 401

<211> 355

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(355)

<223> n = A,T,C or G

<400> 401

actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
 tgatgtctcc aagtagtcca ctttcattta actctttgaa actgtatcat ctttgccaag 120
 taagagtggg ggcctatttc agctgctttg acaaaatgac tggtcctga cttaacgttc 180
 tataaatgaa tgtgtgaag caaagtgcc atggtggcgg cgaagaagan aaagatgtgt 240
 tttgttttgg actctctgtg gtcccttcca atgctgnggg ttccaacca ggggaagggt 300
 cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

139

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

```

atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag cagggtgtgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaagggtggc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgatattg ctgacaactc cttttctgaa gttttactca tttccaa 407

```

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

```

cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaattc aggcacccaa 60
tcctaagcaa gagcctatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcataaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattattttac ataaacctcc attcggtaac catgttgaaa 300
gga 303

```

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

```

aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtto tctcttgatc ctacaaacag 120
acatitttcca ctcggttttc catagttggt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat 225

```

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```

gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgaggggtt tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagttcc tctccttact 120

```

140

```
tcatcccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggg tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatcccac ccct 334
```

<210> 406
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

```
<400> 406
tttcatacct aatgaggagg ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aattnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407
<211> 413
<212> DNA
<213> Homo sapiens

```
<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatacat ggaaacagac aaaaaatatt 120
gtacaacatt gcaccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catittgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagtctc agaaaaagt aaacacagaca atgggccagg ttctgtagta aag 413
```

<210> 408
<211> 183
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G

```
<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggtan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtatcn ccttctnttt tatttactcc ttctgtgcta cccatgtact 180
ntt 183
```

<210> 409
<211> 250
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature

141

<222> (1)...(250)

<223> n = A,T,C or G

<400> 409

```

cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtgggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gccccagga cagcgtgggc tatgtttaca gcgntcctt gctggggggg 240
ggcntatgc                                     250

```

<210> 410

<211> 306

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(306)

<223> n = A,T,C or G

<400> 410

```

ggctgggttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tcccatTTgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aagggtgcttg ctcccccaaga cacatcctaa 180
aagggtgttg aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactgggttg ctttttttgn atctttttta aactggaaa gttcaattgng aaaatgaata 300
tcntgc                                     306

```

<210> 411

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(261)

<223> n = A,T,C or G

<400> 411

```

agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggngaggcaa a                                     261

```

<210> 412

<211> 241

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```

gttcaatggt acctgacatt tctacaacac ccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120

```

142

actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcaactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241

<210> 413
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 413
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtagc cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagttttact tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414
<211> 234
<212> DNA
<213> Homo sapiens

<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggg cttccttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttactatgg,ggggaggtgt attgaagtcc tcca 234

<210> 415
<211> 217
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(217)
<223> n = A,T,C or G

<400> 415
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416
<211> 213
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416

143

```

atgcatatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag                                     213

```

```

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

```

```

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaaag ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttctgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt                                     303

```

```

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

```

```

<400> 418
tttttggcgg tgggtgggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtattttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgctan gattacaggc cgtgagcc                                     328

```

```

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

```

```

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatt 60
acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgtcctt gatcttgctg 120
cttgtttcct ctctgtggct ccattcatag cacagtgtgt gcactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaatt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360

```


144

tggcagccac tcnggctgtg tcgacgcgg

389

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```
gttcctccta actcctgcc aaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccagggc agcaagcctt agccttggtc tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcctgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccg 408
```

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```
gctcaaaaat ctttttactg atnggcattg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacagggtc tttttgggtc cttcttctcc accacnatac acttgcatgc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacagggt tagaaacaag 240
ggtgcaacat gaaattcttg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352
```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```
atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcgcgcg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcgggcggg cataagggct 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttcog ccggtacggc tggcctatga aaattat 337
```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(310)

<223> n = A,T,C or G

<400> 423

145

```

gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tacttgacag aacaggctct ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta                                     310

```

```

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(370).
<223> n = A,T,C or G

```

```

<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggctctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg                                     370

```

```

<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

```

```

<400> 425
aattgctatn ntttattttg ccaactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60
taacaacnca acatcaaggn aananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtnttntg aggagg                                     216

```

```

<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

```

```

<400> 426
cttcagtgga ggataaccct gttgccccgg gccgagggtc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120
gctctctggt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaatgatt tgaagggcc ttaaggaggc cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaaccaat ttgcaactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgcgtg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct      596

```

146

<210> 427
<211> 107
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G

<400> 427
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncaccag 60
cccgggagca gccttanaga gtcctgttt gactgcccgg ctcagn 107

<210> 428
<211> 38
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(38)
<223> n = A,T,C or G

<400> 428
gaacttcna anaangactt tattcactat ttacatt 38

<210> 429
<211> 544
<212> DNA
<213> Homo sapiens

<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcctgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggtggtt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttccact tcagttacac ctactcacc atcctctcct gtgggttctg tgcgtcttca 300
agatactaag ccacattttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gtttagagaga tatgcatatc cagggtttt ttgccagggt gtaggagaga 540
ttat 544

<210> 430
<211> 507
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A,T,C or G

<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccgccaga ctctgattta attgggctgc agtgagaaca 120

147

```

gagcatcaat ttaaaaagct gccagaatg ttntcctggg cagcgttggtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggg ggagaagaag gacccaaaaa agacctgttc 360
tgtcagttaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa

```

```

<210> 431
<211> 392
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct

```

```

<210> 432
<211> 387
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G

```

```

<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgnga gtccagccac tgngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt

```

```

<210> 433
<211> 281
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G

```

```

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60

```

148

```

ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggonctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagngagg ntctctgtnt gccactgggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

```

<210> 434
 <211> 484
 <212> DNA
 <213> Homo sapiens

```

<400> 434
ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca ttccactgtg atgtatatg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtaga tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaacccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctocaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484

```

<210> 435
 <211> 424
 <212> DNA
 <213> Homo sapiens

```

<400> 435
gcgcgcgtca gaggaggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttgagagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaaacctct ggactcccca tgccttaact cccacactct 360
gctatcagaa acttaaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424

```

<210> 436
 <211> 667
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(667)
 <223> n = A,T,C or G

```

<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggggtc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggccaacgt ctgtgcttcg aatataaac 360
tgttcatgtt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420
agttcataat gctgctccat gccagctggg gtgagttggc caaatccttg tggcctatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtc caaacttcaa ctcttggtc agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggggggt gcagctctca 660

```

149

tgttgag

667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

```
ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc aactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attccttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtactcct ctattttcac ccctcttgct tctactctct gccagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
cattttctcca gggtacccta ggtgtcacta ttgggggggac agccagcatc tttagctttc 420
atgttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttggtg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc 693
```

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

```
ctgcttatca caatgaatgt tctcctgggc agcgttggtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta ttcatacctt aatgaggagag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgccca aagaatcttc aagaaggagg 180
actgcaagta tatctgggtg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360
```

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

```
gttctnnta actcctgccca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccaggggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgag 420
aatttagtag t 431
```

<210> 440

<211> 523

<212> DNA

<213> Homo sapiens

150

<400> 440

```

agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tattttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaattgc tgaaatggaa cagattttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata ttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

```

<210> 441

<211> 430

<212> DNA

<213> Homo sapiens

<400> 441

```

gttcctccta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attccttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcgcccgcg 420
aathtagtag 430

```

<210> 442

<211> 362

<212> DNA

<213> Homo sapiens

<400> 442

```

ctaaggaatt agtagtggtc ccatacattg ttggagtggt gctattctaa aagattttga 60
tttcttgaaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aattttatatt gaactgtcaa tgacaaataa aaattccttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362

```

<210> 443

<211> 624

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(624)

<223> n = A,T,C or G

<400> 443

```

tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaacttg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360

```

151

```

taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga ggggaagggtt cctggaaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tattttaaact 600
ttgtccctat ctgctaaaca gatac 624

```

```

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

```

```

<400> 444
gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgtgt gtcagcaaat ccttgaatgc 180
tgcttaagt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacacctg gaagagccaa 360
ggaggcacca gggcataagt gactagactt atggctgacg cggccgcgaa tttagtagta 420
gtaga 425

```

```

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

```

```

<400> 445
catgtttatg ntttttgatt actttgggca cctagtgttt ctaaatcgtc tatcattcct 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatcct caagtctttg 120
tgaaattcct tgcatgtggc agattattgg atgtagtctt cttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtgggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcctctcc tcttgatttt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaaa tgcacgcggc cgcaatttta gtag 414

```

```

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgt 120

```


152

```
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtccctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaacttc caaccttcca ggaaatgcc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttaigtatgg atatatattga 600
aatagtatac attgtcttga tgttttttct g 631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```
ccttgggaaa antntcacia tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggtgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg ccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtta gtacacttcg gtcta 585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(706)

<223> n = A,T,C or G

<400> 449

```
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
```

153

```

ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc. 120
cctggagaggy aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggctgggag cgtcccattc gccattcagg ctgcgcaact 240
gttgggaaggy gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcattgatga cagagtgaat ctccatctta aaaaaaaaaa aaaaaa 706

```

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

```

gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcagggt agtgaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gagggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagtcttta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag 493

```

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 451

```

gggcgcgtcc cattcgccat tcaggctgag caactgttgg gaagggcgat cgggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttccagc cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(51)

<223> n = A,T,C or G

154

<400> 452
agacgggtttc accnttataa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)... (317)
<223> n = A,T,C or G

<400> 453
tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaacccat 120
ttcaccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
taccatgtc tttatta 317

<210> 454
<211> 231
<212> DNA
<213> Homo sapiens

<400> 454
ttcgaggtag aatcaactct cagagtgttag ttctcttcta tagatgagtc agcattaata 60
taagccacgc cagcctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttctcttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455
<211> 231
<212> DNA
<213> Homo sapiens

<400> 455
taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcttttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggtctc tttctcctct a 231

<210> 456
<211> 231
<212> DNA
<213> Homo sapiens

<400> 456
ttggcaggta cccttataaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcggtt attattcttg gagaaacctt gtctgtttac tgtaaccttt 120
tgactcaaa ttcctttatc aggaataact acatagccac tatttataaa gccattggaa 180
cctttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaag t 231

<210> 457
<211> 231
<212> DNA

155

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

```
cgagggtaccc aggggtctga aaatctctnn ttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgatcc 180
agttgtctaa atcgatgcct catttctctt gaggtgtcgc tggcttttgt g 231
```

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

```
aggtctgggt cccccactt cactccct ctactctctc taggactggg ctgggccaaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttcctca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttcaa 180
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<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

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gcctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
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<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

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cccacctccc cacacgcaca cggccagcct ggagccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccacc ctaccaggct taaggataga a 231
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<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

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gtggggttca gtgaggagtg ggaaattgg tccagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtctcag agctgggaat t 231
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<210> 462

156

<211> 231
<212> DNA
<213> Homo sapiens

<400> 462
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gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggttag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463
<211> 231
<212> DNA
<213> Homo sapiens

<400> 463
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catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180
tggggagggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c 231

<210> 464
<211> 231
<212> DNA
<213> Homo sapiens

<400> 464
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aaggacatca catatgaaga atgtttaagt tggagggtggc aacgtgaatt gcaaacaggg 120
cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c 231

<210> 465
<211> 231
<212> DNA
<213> Homo sapiens

<400> 465
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aggatggcac aatttttgct tgtgttcata atatactcag attagtccag ctccatcaga 180
taaactggag acatgcagga cattagggta gtgtttagc tctggtaatg a 231

<210> 466
<211> 231
<212> DNA
<213> Homo sapiens

<400> 466
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cctgtgcaat caaatattgt ggagaattcc ctactggag aagtcacaaa gactataggc 180
aataatggag accagtccca caagatgaca accagtcggt gtgtgcggct g 231

<210> 467
<211> 311
<212> DNA
<213> Homo sapiens

<400> 467

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gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggtctgt ggacgtcagt 240
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ctgcagcaga c                                     311

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<210> 468

<211> 3112

<212> DNA

<213> Homo sapiens

<400> 468

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tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180
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aaatgggata cacagtatga tctataaagt gggatatagt atgatctact tctactgggtt 420
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gattatcatt caatctcata gttttgtcat ggcccaattt atcctcactt gtgcctcaac 600
aaattgaact gttaacaaag gaatctctgg tcctgggtaa tggctgagca ccactgagca 660
tttccattcc agttggcttc ttgggtttgc tagctgcac actagtcac ttaataaaat 720
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tttgtccttg tagttaattg aaagaaatag ggcactcttg tgagccactt taggggttcac 3060
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```

<210> 469

<211> 2229

<212> DNA

<213> Homo sapiens

<400> 469

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tgatttgcca aaattctaaa ggcactcac catgaaatgg ataaaggtta cctttgggga 180
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aacgtgcccc ataaacattc cctctgtggc tcttgcatth catatatthta tctaaactct 360
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ccttctttgc atgaagtaag atagtcaact tattcaaaac ttatcatcat tctagattta 480
agagacaagg aagagcttct caggcagaag gaataatgta tgctgacat gttcaaggaa 540
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aatggaatt 2229

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<210> 470

<211> 2426

<212> DNA

<213> Homo sapiens

<400> 470

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```

<210> 471

<211> 812

<212> DNA

<213> Homo sapiens

<400> 471

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gagatcagat attacaacag ctttgttttg agggtagaa atatgaaatg atttgttat 180
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atttcaaatc tgtaatcccg ttcaataaaa tatccacaac aggatctgtt ttccctgccc 420

```


160

```

tcctttaagg aacacatcaa ttcatTTTTct aatgtccttc cctcacaagc gggaccaggc 480
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gtgcttctt ttgtgcttcc tgtgtgtgtg gatattttaa ggggctggaa atgtgcaaaa 600
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```

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<210> 472
<211> 515
<212> DNA
<213> Homo sapiens

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```

<220>
<221> misc_feature
<222> (1)...(515)
<223> n = A,T,C or G

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<400> 472
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agatgggcag ccataagtta aaaagaagac aagctgaagc tacacacatg gctgatgtca 420
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gaaaaaaaaa naaaaaaaaa aaanaaaaaa aaaaa 515

```

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<210> 473
<211> 5829
<212> DNA
<213> Homo sapiens

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<400> 473
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162

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<210> 474

<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<210> 475

<211> 2414

<212> DNA

<213> Homo sapiens

<220>

163

<221> unsure

<222> (33)

<223> n=A,T,C or G

<400> 475

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<210> 476

<211> 3434

<212> DNA

<213> Homo sapiens

<400> 476

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<210> 477

<211> 140

<212> PRT

<213> Homo sapiens

165

<400> 477

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      20      25      30
Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
      35      40      45
His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
      50      55      60
His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
      65      70      75      80
Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
      85      90      95
Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
      100      105      110
Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
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Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
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<210> 478

<211> 143

<212> PRT

<213> Homo sapiens

<400> 478

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Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
      20      25      30
Gly Glu Ile Thr Trp Thr His His Thr Ile Thr Gly Thr Gln Thr
      35      40      45
His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
      50      55      60
Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
      65      70      75      80
Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
      85      90      95
His Gly His Thr Ser Thr Pro Ser His His Thr His Cys Leu Trp
      100      105      110
Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
      115      120      125
His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
      130      135      140

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<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

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Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
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Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
      20      25      30

```

166

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
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 His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
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 Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
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 Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
 85 90 95
 His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
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 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
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 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
 165 170 175
 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
 180 185 190
 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
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 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
 210 215 220

<210> 480

<211> 144

<212> PRT

<213> Homo sapiens

<400> 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
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 20 25 30
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
 35 40 45
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
 50 55 60
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
 65 70 75 80
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
 85 90 95
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
 100 105 110
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
 115 120 125
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
 130 135 140

<210> 481

<211> 167

<212> PRT

<213> Homo sapiens

<400> 481

167

```

Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
      5      10      15
Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
      20      25      30
Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
      35      40      45
Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
      50      55      60
Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro
      65      70      75      80
Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg
      85      90      95
Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala
      100      105      110
Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His
      115      120      125
Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe
      130      135      140
Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser
      145      150      155      160
Trp Leu Ser Arg Gly Arg Pro
      165

```

<210> 482

<211> 143

<212> PRT

<213> Homo sapiens

<400> 482

```

Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val
      5      10      15
Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
      20      25      30
Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
      35      40      45
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
      50      55      60
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
      65      70      75      80
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
      85      90      95
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
      100      105      110
Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
      115      120      125
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
      130      135      140

```

<210> 483

<211> 143

<212> PRT

<213> Homo sapiens

<400> 483

```

Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5      10      15
Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala

```


168

```

      20      25      30
Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35      40      45
Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50      55      60
Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65      70      75      80
Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85      90      95
Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100      105      110
Arg Leu Val Gln Ala Glu His Pro Pro His Pro Leu Glu Glu Val
      115      120      125
Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130      135      140

```

<210> 484
 <211> 30
 <212> PRT
 <213> Homo Sapien

```

      <400> 484
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1      5      10      15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20      25      30

```

<210> 485
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

```

      <400> 485
gggaagctta tcacctatgt gccgcctctg c

```

31

<210> 486
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

```

      <400> 486
gcgaattctc acgctgagta tttagcc

```

27

<210> 487
 <211> 36
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 487

169

cccgaattct tagctgccca tccgaacgcc ttcac

36

<210> 488
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 488

gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 489

Met	Asp	Arg	Leu	Val	Gln	Arg	Phe	Gly	Thr	Arg	Ala	Val	Tyr	Leu	Ala
1				5					10					15	
Ser	Val	Ala													

<210> 490
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 490

Tyr	Leu	Ala	Ser	Val	Ala	Ala	Phe	Pro	Val	Ala	Ala	Gly	Ala	Thr	Cys
1				5					10					15	
Leu	Ser	His	Ser												
			20												

<210> 491
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 491

Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
1				5					10					15	
Thr	Gly	Phe	Thr												
			20												

<210> 492
<211> 20
<212> PRT

170

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 495

Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu	Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro
1				5					10					15	
Phe	Pro	Asn	Gly												
			20												

<210> 496

<211> 21

<212> PRT

<213> Artificial Sequence

171

<220>

<223> Made in a lab

<400> 496

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5					10					15	
Pro	Pro	Pro	Pro	Ala											
				20											

<210> 497

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 497

Leu	Leu	Pro	Pro	Pro	Pro	Ala	Leu	Cys	Gly	Ala	Ser	Ala	Cys	Asp	Val
1				5					10					15	
Ser	Val	Arg	Val												
			20												

<210> 498

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 498

Asp	Val	Ser	Val	Arg	Val	Val	Val	Gly	Glu	Pro	Thr	Glu	Ala	Arg	Val
1				5					10					15	
Val	Pro	Gly	Arg												
			20												

<210> 499

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5					10					15	
Ser	Ala	Phe	Leu												
			20												

<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

172

<223> Made in a lab

<400> 500

Leu	Asp	Ser	Ala	Phe	Leu	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met
1				5					10					15	
Gly	Ser	Ile	Val												
			20												

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

Phe	Met	Gly	Ser	Ile	Val	Gln	Leu	Ser	Gln	Ser	Val	Thr	Ala	Tyr	Met
1				5					10					15	
Val	Ser	Ala	Ala												
			20												

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(414)

<223> n=A,T,C or G

<400> 502

caccatggag	acaggcctgc	gctggctttt	cctggctcgt	gtgctcaaag	gtgtccaatg	60
tcagtcggtg	gaggagtccg	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttgaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
agggaagggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnatnt	ccaaaacctn	gaccacggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatttttg	tggcagaatg	aatactggta	atagtgggtg	360
gaagaatatt	tggggcccag	gcaccctggt	caccgtnctc	tcagggcaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(379)

<223> n=A,T,C or G

<400> 503

atncgatggt	gcttgggtcaa	aggtgtccag	tgctcagtcg	tggaggagtc	cggggggtcgc	60
ctgggtcacgc	ctgggacacc	cctgacactc	acctgcaccg	tntctggatt	ngacatcagt	120
agctatggag	tgagtgggtg	ccgccaggct	ccagggaagg	ggctgggnata	catcgggatca	180
ttagtagtag	tggtacattt	tacgcgagct	gggcgaaagg	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	agggggggtt	aattataaag	acatttgggg	cccaggcacc	ctggtcaccg	360

173

tntocttagg gcaacctaa

379

<210> 504
 <211> 19
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 504
 Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu
 1 5 10 15
 Asn Ser Ala

<210> 505
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 505
 Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr
 1 5 10 15
 Asn Thr Ala Asn
 20

<210> 506
 <211> 407
 <212> DNA
 <213> Homo Sapien

<400> 506
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaaggtgt ccagtgtcag 60
 tcgctggagg agtccggggg tcgcctggtc acgcctggga caccctgac actcacctgc 120
 accgtctctg gattctccct cagtagcaat gcaatgatct gggtccgcca ggctccaggg 180
 aaggggctgg aatacatcgg atacattagt tatggtggta gcgcatacta cgcgagctgg 240
 gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt 300
 ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg 360
 ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa 407

<210> 507
 <211> 422
 <212> DNA
 <213> Homo Sapien

<400> 507
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaaggtgt ccagtgtcag 60
 tcgctggagg agtccggggg tcgcctggtc acgcctggga caccctgac actcacctgt 120
 acagtctctg gattctccct cagcaactac gacctgaact gggtccgcca ggctccaggg 180
 aaggggctgg aatggatcgg gatcattaat tatggtggta ggacggacta cgcgaactgg 240
 gcaaaaggcc gggtcaccat ctccaaaacc tcgaccacgg tggatctcaa gatcgccagt 300
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360
 ggtccgtgct tgcgcatctg gggcccaggc accctgggtc cgtctctctt agggcaacct 420

174

aa

422

<210> 508
 <211> 411
 <212> DNA
 <213> Homo Sapien

 <220>
 <221> misc_feature
 <222> (1)...(411)
 <223> n=A,T,C or G

<400> 508
 atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaaggtgtc cagtgtcagt 60
 cgggtggagga gtccgggggt cgcttggtca cgcctgggac acccctgaca ctcacctgca 120
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180
 aggggctgga atggatcgga atcattggta ctctgggtga cacatactac gcgaggtggg 240
 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360
 ctggttatta taaaatctgg ggcccaggca ccctgggtcac cgtctccttg g 411

<210> 509
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 509
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 510
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 510
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5 10 15

<210> 511
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
 1 5 10 15

175

<210> 512
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 512
 Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
 1 5 10 15

<210> 513
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 513
 Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
 1 5 10 15

<210> 514
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 514
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 515
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 515
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
 1 5 10 15

<210> 516
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 516
 Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln


```

1           5           10           15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1           5           10           15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1           5           10           15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1           5           10           15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 520
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
1           5           10           15
Glu Ala Arg Arg His Tyr Asp Glu Gly
20          25

<210> 521
<211> 21
<212> PRT
<213> Artificial Sequence

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177

<220>

<223> Made in a lab

<400> 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5					10					15	
Pro	Pro	Pro	Pro	Ala											
				20											

<210> 522

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

<210> 523

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<220>

<221> VARIANT

<222> (1)...(254)

<223> Xaa = any amino acid

<400> 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5					10					15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20					25					30		
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
			35				40					45			
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln
			50			55					60				
Trp	Val	Leu	Ser	Ala	Thr	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly
65					70				75					80	
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met
			85					90						95	
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu
			100				105					110			
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu
			115				120				125				
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala
			130			135					140				
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg
145					150					155					160

178

Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524

<211> 765

<212> DNA

<213> Homo sapien

<400> 524

atggccacag	caggaaatcc	ctggggctgg	ttcctggggt	acctcatcct	tggtgtcgca	60
ggatcgctcg	tctctggtag	ctgcagccaa	atcataaacg	gcgaggactg	cagcccgcac	120
tcgcagccct	ggcaggcggc	actgggtcatg	gaaaacgaat	tgttctgctc	gggcgtcctg	180
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	240
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	300
ctctccgtac	ggcacccaga	gtacaacaga	cccttgctcg	ctaacgacct	catgctcatc	360
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatcagcat	tgcttcgcag	420
tgccctaccg	cgggggaactc	ttgcctcggt	tctggctggg	gtctgctggc	gaacggcaga	480
atgcctaccg	tgctgcagtg	cgtgaacgtg	tcgggtggtg	ctgaggaggt	ctgcagtaag	540
ctctatgacc	cgctgtacca	cccagcatg	ttctgcgccg	gcggagggca	agaccagaag	600
gactcctgca	acggtgactc	tgggggggccc	ctgatctgca	acgggtactt	gcagggcctt	660
gtgtcttttcg	gaaaagcccc	gtgtggccaa	gttggcgtgc	caggtgtcta	caccaacctc	720
tgcaaattca	ctgagtggat	agagaaaacc	gtccaggcca	gttaa		765

<210> 525

<211> 254

<212> PRT

<213> Homo sapien

<400> 525

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
 1 5 10 15
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
 20 25 30
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
 35 40 45
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60
 Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg

179

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145          150          155          160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
          165          170          175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
          180          185          190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly
          195          200          205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
          210          215          220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
          225          230          235          240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
          245          250

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<210> 526

<211> 963

<212> DNA

<213> Homo sapiens

<400> 526

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atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60
aaagcccat tctgggttgg ctccccctc ctttccatgt atgtagtggc aatgtttgga 120
aactgcatcg tggcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttcgagc cattgacctg gccttatcca catccaccat gcctaagatc 240
cttgcccttt tctggtttga ttcccgagag attagctttg aggcctgtct taccagatg 300
ttctttattc atgccctctc agccattgaa tccaccatcc tgctggccat ggcctttgac 360
cgttatgtgg ccatctgcca cccactgcgc catgctgcag tgctcaaca tacagtaaca 420
gccagattg gcatcggtgg tgtggtccgc ggatccctct tttttttccc actgcctctg 480
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<210> 527

<211> 320

<212> PRT

<213> Homo sapiens

<400> 527

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Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile
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Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser
          20          25          30
Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val
          35          40          45
Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
          50          55          60
Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
          65          70          75          80
Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys
          85          90          95
Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
          100          105          110

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180

```

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
    115                120                125
Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
    130                135                140
Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
    145                150                155                160
Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
    165                170                175
Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
    180                185                190
Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
    195                200                205
Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
    210                215                220
Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
    225                230                235                240
Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
    245                250                255
Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
    260                265                270
Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
    275                280                285
Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
    290                295                300
Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys
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<210> 528
<211> 20
<212> DNA
<213> Homo Sapien

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<400> 528
actatggtcc agaggtgtg

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20

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<210> 529
<211> 20
<212> DNA
<213> Homo Sapien

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<400> 529
atcacctatg tgccgcctct

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20

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<210> 530
<211> 1852
<212> DNA
<213> Homo sapiens

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<400> 530
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tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240
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ggagttcttc cttcatagtt catccatatg gctccagagg aaaattatat tattttgtta 480
tggtatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 540

```

181

```

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gctttctcca ccttgctgga agtgacctgc tgtccagaag tttgatggct gaggagtata 720
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<210> 531
 <211> 879
 <212> DNA
 <213> Homo sapiens

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<400> 531
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tgcaagtggg gctgccactg cttcccctgc tgcaggggga gcggcaagag caacgtgggc 180
gcttggggag actacgatga cagcgccctc atggatccca ggtaccacgt ccatggagaa 240
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gtcatgctca gggacacgga tgtgaacaag agggacaagc aaaagaggac tgctctacat 360
ctggcctctg ccaatgggaa ttcagaagta gtaaaactcg tgctggacag acgatgtcaa 420
cttaatgtcc ttgacaacaa aaagaggaca gctctgacaa aggcctgaca atgccaggaa 480
gatgaatgtg cgttaatgtt gctggaacat ggcactgatc caaatattcc agatgagtat 540
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<210> 532
 <211> 292
 <212> PRT
 <213> Homo sapiens

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<400> 532
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Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
          20                25                30
Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
          35                40                45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp

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182

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      50      55      60
Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
 65      70      75      80
Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
      85      90      95
Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
      100      105      110
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
      115      120      125
Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
      130      135      140
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
145      150      155      160
Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
      165      170      175
Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
      180      185      190
Asp Lys Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu
      195      200      205
Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
      210      215      220
Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
225      230      235      240
Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
      245      250      255
Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
      260      265      270
Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
      275      280      285
Val Ile Ile Met
      290

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<210> 533
 <211> 801
 <212> DNA
 <213> Homo sapiens

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<400> 533
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tatgccactg cagcattctt gggtgccaag aggccaaacca caggccatct tgagaaggag 180
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cctgcagcga gtgaggttg tggctgtgcc cccagctcct ggcacaccct cgcagaggtg 600
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tgccaagag gcagaccata g
      801

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<210> 534
 <211> 266
 <212> PRT
 <213> Homo sapiens

183

<400> 534

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Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala
      20      25      30
Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
      35      40      45
Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
      50      55      60
Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
      65      70      75      80
Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
      85      90      95
Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
      100      105      110
Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
      115      120      125
Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
      130      135      140
Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
      145      150      155      160
Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr
      165      170      175
Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser
      180      185      190
Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
      195      200      205
Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
      210      215      220
Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
      225      230      235      240
Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu
      245      250      255
Trp Ala Ser Trp Leu Pro Arg Gly Arg Pro
      260      265

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<210> 535

<211> 6082

<212> DNA

<213> Homo sapiens

<400> 535

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gcaagatgct gccgtgtac caggagtgta agcccaaccc gctgcaggac gcgaacctct 240
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ttcgtcttag taacatggcc atggggaaga caaccacagg ccagatagtc aatctgctgt 780
ccaatgatgt gaacaagttt gatcagtgta cagtgttctt acacttctg tgggcaggac 840

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185

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<210> 536

<211> 6140

<212> DNA

<213> Homo sapiens

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<210> 537

<211> 1228

<212> PRT

<213> Homo sapiens

<400> 537

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<210> 538

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<213> Homo sapiens

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 100 105 110
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
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 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
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 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
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 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
 225 230 235 240
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
 245 250 255
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
 260 265 270
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile

				740					745					750		
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	
		755					760					765				
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	
		770					775					780				
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	
785					790					795					800	
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	
			805						810					815		
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	
			820					825					830			
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	
		835					840					845				
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	
		850				855					860					
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	
865					870					875					880	
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	
			885					890						895		
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	
			900					905					910			
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	
		915					920					925				
-Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	
		930				935					940					
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	
945					950					955					960	
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	
			965					970						975		
Glu	Lys	Glu	Ala	Pro	Trp	Glu	Tyr	Gln	Lys	Arg	Pro	Pro	Pro	Ala	Trp	
			980					985					990			
Pro	His	Glu	Gly	Val	Ile	Ile	Phe	Asp	Asn	Val	Asn	Phe	Met	Tyr	Ser	
		995					1000					1005				
Pro	Gly	Gly	Pro	Leu	Val	Leu	Lys	His	Leu	Thr	Ala	Leu	Ile	Lys	Ser	
		1010				1015					1020					
Gln	Glu	Lys	Val	Gly	Ile	Val	Gly	Arg	Thr	Gly	Ala	Gly	Lys	Ser	Ser	
1025					1030					1035					1040	
Leu	Ile	Ser	Ala	Leu	Phe	Arg	Leu	Ser	Glu	Pro	Glu	Gly	Lys	Ile	Trp	
			1045						1050					1055		
Ile	Asp	Lys	Ile	Leu	Thr	Thr	Glu	Ile	Gly	Leu	His	Asp	Leu	Arg	Lys	
			1060				1065					1070				
Lys	Met	Ser	Ile	Ile	Pro	Gln	Glu	Pro	Val	Leu	Phe	Thr	Gly	Thr	Met	
		1075	</													

193

				1205					1210					1215					
Val	Leu	Leu	Gln	Asn	Lys	Glu	Ser	Leu	Phe	Tyr	Lys	Met	Val	Gln	Gln				
			1220					1225					1230						
Leu	Gly	Lys	Ala	Glu	Ala	Ala	Ala	Leu	Thr	Glu	Thr	Ala	Lys	Gln	Arg				
		1235				1240						1245							
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<210> 539
<211> 10
<212> PRT
<213> Artificial Sequence
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<220>
<223> Made in a lab

<400> 539
Cys Leu Ser His Ser Val Ala Val Val Thr
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<210> 540
<211> 9
<212> PRT
<213> Artificial Sequence
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<220>
<223> Made in a lab

<400> 540
Ala Val Val Thr Ala Ser Ala Ala Leu
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<210> 541
<211> 14
<212> PRT
<213> Homo sapiens
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<400> 541
Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
5 10

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<210> 542
<211> 15
<212> PRT
<213> Homo sapiens
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<400> 542
Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
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<210> 543
<211> 12
<212> PRT
<213> Homo sapiens
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<400> 543
Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val
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194

<210> 544
 <211> 18
 <212> PRT
 <213> Homo sapiens

<400> 544
 Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe
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 Met Thr

<210> 545
 <211> 18
 <212> PRT
 <213> Homo sapiens

<400> 545
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
 5 10 15
 Ser Val

<210> 546
 <211> 29
 <212> PRT
 <213> Homo sapiens

<400> 546
 Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly
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 Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
 20 25

<210> 547
 <211> 58
 <212> PRT
 <213> Homo sapiens

<400> 547
 Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu
 5 10 15
 Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
 20 25 30
 Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
 35 40 45
 Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
 50 55

<210> 548
 <211> 18
 <212> PRT
 <213> Homo sapiens

<400> 548
 Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

195

Glu Cys 5 10 15

<210> 549
 <211> 18
 <212> PRT
 <213> Homo sapiens

<400> 549
 Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg
 5 10 15
 Gln Ala

<210> 550
 <211> 14
 <212> PRT
 <213> Homo sapiens

<400> 550
 Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe
 5 10

<210> 551
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 551
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<210> 552
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 <212> DNA
 <213> Homo sapiens

<400> 552
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 agccaaggaa gcttcacctg tacttacagc cacacgcat ggctcatatt acagcctgaa 240
 ctctgcctcc actcagatca gtgataacat tagaaactca ttggagcacg aaccctgttg 300
 tgaactgcct atccgaagga tctaggttgt gtgcttcgta tgagaatcta atgccagatg 360
 atctatcatt gtctcacttt gccccagat aagaccatct agttgcagaa aaataagctc 420
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 ttttacacat gcctagtgat gcttcatgga caaggcttgg ctctgttgag tccaactaac 540
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 ggtcactcaa ggggccaacc acagctggga gccactgctc aggggaaggt tcatatggga 720
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<210> 553

<211> 58

<212> PRT

<213> Homo sapiens

<400> 553

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Ser Ile Cys Asn Met Thr Cys Ala Ser Val Phe Phe Cys Asp Gln Lys
              5              10              15
Phe Leu Thr Phe Ser Phe Leu Ser Met Val Glu Pro Pro Arg Ala Gly
              20              25              30
Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
              35              40              45
Glu Pro His His Thr Gly Gly Gly Glu His
              50              55

```

<210> 554

<211> 59

<212> PRT

<213> Homo sapiens

<400> 554

```

Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
              5              10              15
Cys Ala Ala Glu Ala Ser Thr Lys Pro Tyr Phe Tyr Thr Cys Leu Val
              20              25              30
Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
              35              40              45
Glu Ile Leu Arg Phe Leu Phe Asn Gly Phe Leu
              50              55

```

197

<210> 555
 <211> 71
 <212> PRT
 <213> Homo sapiens

<400> 555
 Leu Gly Arg Phe Ser Leu Ser Cys Lys Ser Gly His Ser Arg Gly Gln
 5 10 15
 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser
 20 25 30
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp
 35 40 45
 Leu Val Ala Lys Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro
 50 55 60
 Ser Asp Pro Leu Glu Leu Leu
 65 70

<210> 556
 <211> 81
 <212> PRT
 <213> Homo sapiens

<400> 556
 Asn His Pro Glu Gln Gly Ser Ser Thr Pro Arg Pro Gln Thr His Thr
 5 10 15
 Ser Pro Arg Thr Ile Met Asn His Thr Thr Gln Glu Glu Val Ser Thr
 20 25 30
 Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly
 35 40 45
 Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile
 50 55 60
 Arg Asn Ser Leu Glu His Glu Pro Cys Cys Glu Leu Pro Ile Arg Arg
 65 70 75 80
 Ile

<210> 557
 <211> 54
 <212> PRT
 <213> Homo sapiens

<400> 557
 Ser Leu Ser Ala Thr Pro Leu Thr Leu Trp Asn Ser Ser Asp Pro Leu
 5 10 15
 Glu Gln Ala Tyr Leu Ile Ser Ala Arg Glu Lys Thr Asn Asn Gly Leu
 20 25 30
 Lys Gly Ser Leu Thr Met Lys Val Ser Ala Asn Ser Trp Leu Arg Cys
 35 40 45
 Gly Phe His Ile Arg Phe
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<210> 558
 <211> 77
 <212> PRT
 <213> Homo sapiens

198

<220>

<221> VARIANT

<222> (1)...(77)

<223> Xaa = Any amino acid

<400> 558

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Asn Asp Arg Asp Arg Asn Ser Asn Lys Val Ile Xaa Lys Ala Asn Leu
      5              10              15
Ile Tyr Phe Thr Asn Leu Thr Ser Cys Leu Ser Val Gln Asn Gln Thr
      20              25              30
Phe Thr Cys Thr Lys Arg His Lys His Leu Gln Cys Ser Ser Val His
      35              40              45
Leu Cys Lys Ile Pro Pro Arg Leu Lys Gly Arg Asp Lys Lys Lys Lys
      50              55              60
Pro Ser Tyr Leu Ser Gly Val Leu His Ser Arg Ser Tyr
      65              70              75

```

<210> 559

<211> 50

<212> PRT

<213> Homo sapiens

<400> 559

```

Thr Leu Pro Pro Leu Arg Ser Val Ile Thr Leu Glu Thr His Trp Ser
      5              10              15
Thr Asn Pro Val Val Asn Cys Leu Ser Glu Gly Ser Arg Leu Cys Ala
      20              25              30
Ser Tyr Glu Asn Leu Met Pro Asp Asp Leu Ser Leu Ser His Phe Ala
      35              40              45
Pro Arg
      50

```

<210> 560

<211> 56

<212> PRT

<213> Homo sapiens

<400> 560

```

Ile Gly Ser Leu Lys Gly Pro Thr Thr Ala Gly Ser His Cys Ser Gly
      5              10              15
Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr
      20              25              30
Lys Gly Ala Ser Gln Tyr Arg Ser Gly Ser Lys Glu Glu Glu Thr Asn
      35              40              45
Thr Asp Leu Phe Leu Pro Pro Leu
      50              55

```

<210> 561

<211> 57

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

199

<222> (1)...(57)

<223> Xaa = Any amino acid

<400> 561

```

Val Leu His Leu Asp Gln Met Asn Asn Val Gly Ile Xaa Met Asp Lys
              5              10              15
Gly Leu Lys Ser Pro Glu Ile Lys Asn Pro Ala Pro Thr Gly Thr Ser
              20              25              30
Asn Leu Ser Cys Phe Leu Ser Xaa Phe Trp Leu Met Gln Gly Thr Asn
              35              40              45
Ser Leu Pro Arg Glu Asn Tyr Leu Asn
              50              55

```

<210> 562

<211> 59

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> (1)...(59)

<223> Xaa = Any amino acid

<400> 562

```

Asp Leu Tyr Pro Xaa Arg Ser Gln His Cys Ser Phe Asp Pro Ser Val
              5              10              15
Ala Pro Met His Gly Ile Lys Asn Ser Ile Thr Ser Leu Ile Phe Leu
              20              25              30
Ile Ser Tyr Leu Xaa Leu Glu Met Ser Ser Leu Ser Glu Ser Leu Val
              35              40              45
Leu Ser Ser Gly Asp Tyr Val Leu Asp Thr Pro
              50              55

```

<210> 563

<211> 79

<212> PRT

<213> Homo sapiens

<400> 563

```

Cys Phe Leu Phe Pro Tyr Leu Trp Leu Tyr Ala Gln Pro Leu Phe Pro
              5              10              15
Lys Gln Gln Pro Pro Ala Leu Ala Pro Gly His Pro Asp Phe Ile His
              20              25              30
Thr Gln Asn Glu Gln Ile Asp Pro Ser Pro His Ile Gln Asn Leu Met
              35              40              45
Trp Asn Pro His Leu Ser Gln Glu Leu Ala Glu Thr Phe Met Val Arg
              50              55              60
Asp Pro Leu Arg Pro Leu Leu Val Phe Ser Leu Ala Asp Ile Arg
              65              70              75

```

<210> 564

<211> 64

<212> PRT

<213> Homo sapiens

<400> 564

200

```

Ala Cys Ser Lys Gly Ser Glu Glu Phe Gln Arg Val Arg Gly Val Ala
      5              10              15
Glu Arg Asp Gln Cys Leu Phe Leu Leu Leu Cys Tyr Gln Ile Tyr Thr
      20              25              30
Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser
      35              40              45
His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro
      50              55              60

```

<210> 565
 <211> 57
 <212> PRT
 <213> Homo sapiens

<220>
 <221> VARIANT
 <222> (1)...(57)
 <223> Xaa = Any amino acid

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<400> 565
Leu Tyr Tyr Cys Ser Tyr Leu Cys His Phe Arg Thr Ala Leu Ile Leu
      5              10              15
Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln
      20              25              30
Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu
      35              40              45
Tyr Ala Val Ser Ser Xaa His Asn Val
      50              55

```

<210> 566
 <211> 55
 <212> PRT
 <213> Homo sapiens

```

<400> 566
Ile Leu Leu Glu Phe Phe Arg Asn Gln Arg Gly Ser Leu Asn Pro Arg
      5              10              15
Lys Thr Val Pro Phe Ile Lys Ser Glu Gly Gly Glu Lys Lys Gly His
      20              25              30
Cys Asn His Ser Val Val Ser Ile Asp Ser Ala Ala Ala Leu Leu Pro
      35              40              45
Leu Lys Leu Val Leu Leu Pro
      50              55

```

<210> 567
 <211> 51
 <212> PRT
 <213> Homo sapiens

```

<400> 567
Tyr Ser Asp Phe Asp Val Phe Cys Ser His Thr Tyr Gly Tyr Met Leu
      5              10              15
Ser His Cys Ser Gln Ser Ser Ser Pro Leu Leu Trp Pro Leu Gly Ile
      20              25              30
Leu Thr Leu Ser Thr His Lys Met Ser Lys Leu Thr Leu Pro Pro Ile

```

201

35 40 45
 Phe Arg Thr
 50
 <210> 568
 <211> 75
 <212> PRT
 <213> Homo sapiens
 <400> 568
 Lys Val Gly Glu Tyr Ile Leu Gln Ser Leu Leu Arg Ile Arg Lys Ile
 5 10 15
 Tyr Val Ala Phe Asn Ser Val Pro Ser Thr Cys Leu Leu Ala Ser Leu
 20 25 30
 Thr Glu Thr Pro Val Thr Thr Ile Leu Thr Ile Ile Ile Asn Leu Thr
 35 40 45
 Cys Phe Gln His Ala Glu Ser Ser Tyr Leu Phe Tyr Pro Leu Ala Asp
 50 55 60
 Phe Leu Leu Gln His Ile Ser Leu Gly Lys Leu
 65 70 75

<210> 569
 <211> 4809
 <212> DNA
 <213> Homo sapiens

<400> 569
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```

<210> 570

<211> 951

<212> DNA

<213> Homo sapiens

<400> 570

203

```

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ccatttttagt actatgggtg agtacatgga attgaagtct ggcttaaate ttcagaaagt 180
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```

<210> 571
 <211> 819
 <212> DNA
 <213> Homo sapiens

```

<400> 571
cagcttaaaa atggtttctt gaaatcagtg attagcattc actcaccagt acccctacta 60
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gaaagatggt tctcaggttt ttccctgacg attttcttct tttctgattc tgacaatggt 300
ttaaatcatt gtactgtggt tatcatttct ctgcatttat ttaccatc ttcccttgta 360
acttgtccta ttgtctttta atttctgcct gttctttatg gctttcaact tcataaataa 420
catgttttct caaatctctt tgtgaattcc agagagggcc aggcacgggt gctcacatct 480
gtaatcccag cactttgggg aggtcgagac ggggtggatca cttgaggtca ggagtttgag 540
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tggtggcggg cgctgtaat cccagggtact cgggaggctg agggaggaga atcgcttgaa 660
ctgaggaggc tgaggaggga gaatcgcttg aacccgggag gcagaggttg cagtgaaccg 720
agatcatggt gctgcactcc agcctggtca acagagcaag actctgcctc aaaaacaaac 780
aaataacaa acaaacaaac aaaacagaga gattttgct 819

```

<210> 572
 <211> 203
 <212> DNA
 <213> Homo sapiens

```

<400> 572
tatagaatac tcaagctatg catcaagctt ggtaccgagc tcggatccac tatttacggc 60
cgccagtgtg ctggaattcg cccttagctc ggatccacta gtccagtgtg gtggaattcc 120
attgtgttgg gcccaacaca atggagccac cacatccagc ctgccacata cttttaact 180
atcaggtctc atgagaactc atg 203

```

<210> 573
 <211> 132
 <212> PRT
 <213> Homo sapiens

```

<400> 573
Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
          5                      10                      15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg

```

204

```

      20      25      30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
      35      40      45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
      50      55      60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
      65      70      75      80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
      85      90      95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
      100      105      110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
      115      120      125
Leu Leu Asn Tyr
      130

```

<210> 574
 <211> 62
 <212> PRT
 <213> Homo sapiens

```

<400> 574
Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
      5      10      15
His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
      20      25      30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Glu
      35      40      45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
      50      55      60

```

<210> 575
 <211> 76
 <212> PRT
 <213> Homo sapiens

```

<400> 575
Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
      5      10      15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
      20      25      30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
      35      40      45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
      50      55      60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
      65      70      75

```

<210> 576
 <211> 68
 <212> PRT
 <213> Homo sapiens

<220>
 <221> VARIANT

205

<222> (1)...(68)

<223> Xaa = Any Amino Acid

<400> 576

```

Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr
      5              10              15
Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
      20              25              30
Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
      35              40              45
Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
      50              55              60
Pro Gly Tyr Ser
65

```

<210> 577

<211> 57

<212> PRT

<213> Homo sapiens

<400> 577

```

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
      5              10              15
Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
      20              25              30
Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
      35              40              45
Arg Leu Ala Pro Pro Ala Asp Thr Pro
      50              55

```

<210> 578

<211> 51

<212> PRT

<213> Homo sapiens

<400> 578

```

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
      5              10              15
His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr
      20              25              30
Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr
      35              40              45
Gln Pro His
50

```

<210> 579

<211> 56

<212> PRT

<213> Homo sapiens

<400> 579

```

Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
      5              10              15
Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
      20              25              30
Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
      35              40              45
Ile Ala Lys Val Tyr Gln Pro His

```

206

50

55

<210> 580

<211> 67

<212> PRT

<213> Homo sapiens

<400> 580

```

Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
              5              10              15
Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
              20              25              30
Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
              35              40              45
His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
              50              55              60
Phe Ile His
              65

```

<210> 581

<211> 77

<212> PRT

<213> Homo sapiens

<400> 581

```

Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
              5              10              15
Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
              20              25              30
Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
              35              40              45
Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
              50              55              60
Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
              65              70              75

```

<210> 582

<211> 51

<212> PRT

<213> Homo sapiens

<400> 582

```

Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
              5              10              15
Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
              20              25              30
Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
              35              40              45
Leu Gly Val
              50

```

<210> 583

<211> 60

<212> PRT

<213> Homo sapiens

<400> 583

```

Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg

```

207

```

          5          10          15
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          20          25          30
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          35          40          45
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          50          55          60

```

<210> 584

<211> 76

<212> PRT

<213> Homo sapiens

<400> 584

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

<210> 585

<211> 50

<212> PRT

<213> Homo sapiens

<400> 585

```

Met Val Tyr Arg Phe Gly Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu
          5          10          15
Ala Ser Leu Gly Ser Ser Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp
          20          25          30
Arg Gln Ala Asp Pro Ser Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu
          35          40          45
Leu Phe
          50

```

<210> 586

<211> 60

<212> PRT

<213> Homo sapiens

<400> 586

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

<210> 587

<211> 1408

<212> DNA

<213> Homo sapiens

<400> 587

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cggctggaat tgctctgggt atgatgacag agaaaatgat ctcttcctct gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
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gtgtcagaaa caggagaaaa ttgaagtcac gtctttgggt cgatgtcaag ataacacaac 660
tacaactact aagtctgaag atgggcatta tgcaagaaca gattatgcag agaattgtaa 720
caaattagaa gaaagtgccg gagaacacca cataccttgt ccggaacatt acaatggctt 780
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tacagtatta tagacaaaag aataagacaa gagatctaca catgttgctt tgcatttgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatatat gattatgtat ggatatat 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320
caatawagtt ttttctttcc catgtatttg ttatatataa taaatactca gtgatgagaa 1380
aaaaaaaaa aaaaaaaaaa rwmgaccc 1408

```

<210> 588

<211> 81

<212> PRT

<213> Homo sapiens

<400> 588

```

Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
                    5                      10                      15
Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
                    20                      25                      30
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
                    35                      40                      45
Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
                    50                      55                      60
Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
                    65                      70                      75                      80
Ile

```

<210> 589

<211> 157

<212> PRT

<213> Homo sapiens

<400> 589

```

Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
                    5                      10                      15
Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
                    20                      25                      30
Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu

```

209

```

      35      40      45
Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
  50      55      60
Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
  65      70      75      80
Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
      85      90      95
Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
      100      105      110
Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
      115      120      125
Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
      130      135      140
Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
145      150      155

```

<210> 590

<211> 347

<212> PRT

<213> Homo sapiens

<400> 590

```

Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
      5      10      15
Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
      20      25      30
Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
      35      40      45
Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
      50      55      60
Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
      65      70      75      80
Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
      85      90      95
Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
      100      105      110
Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
      115      120      125
Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
      130      135      140
Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
145      150      155      160
Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
      165      170      175
Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
      180      185      190
Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr Thr
      195      200      205
Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu Asn Ala
      210      215      220
Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys Pro Glu
225      230      235      240
His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser Ile Asn
      245      250      255
Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly Gln His
      260      265      270
Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly Pro Val

```

210

```

      275              280              285
Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile Gln Ile
  290              295              300
Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys Pro Arg
  305              310              315              320
Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr Ser Ser
      325              330              335
Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      340              345

```

<210> 591
 <211> 565
 <212> DNA
 <213> Homo sapien

```

<400> 591
actaaagcaa atgaacaagc tgacttgcta gtatcatctg cattcattga agcacaagaa      60
cttcatgcct tgactcatgt aaatgcaata ggattaaaaa ataaatttga tatcacatgg      120
aaacagacaa aaaatattgt acaacattgc acccagtgtc agattctaca cctggccact      180
caggaagcaa gagttaatcc cagaggtcta tgtcctaata tgttatggca aatggatgtc      240
atgcacgtac cttcatttgg aaaattgtca tttgtocatg tgacagtga tacttattca      300
catttcatat gggcaacctg ccagacagga gaaagtactt cccatgttaa aagacattta      360
ttatcttggt ttcctgtcat gggagttcca gaaaaagtta aaacagacaa tgggccaggt      420
tactgtagta aagcatttca aaaattctta aatcagtgga aaattacaca tacaatagga      480
attctctata attcccaagg acaggccata attgaaggaa ctaatagaac actcaaagct      540
caattggtta aacaaaaaaaa aaaaaa      565

```

<210> 592
 <211> 188
 <212> PRT
 <213> Homo sapien

```

<400> 592
Thr Lys Ala Asn Glu Gln Ala Asp Leu Leu Val Ser Ser Ala Phe Ile
  1              5              10              15
Glu Ala Gln Glu Leu His Ala Leu Thr His Val Asn Ala Ile Gly Leu
      20              25              30
Lys Asn Lys Phe Asp Ile Thr Trp Lys Gln Thr Lys Asn Ile Val Gln
      35              40              45
His Cys Thr Gln Cys Gln Ile Leu His Leu Ala Thr Gln Glu Ala Arg
      50              55              60
Val Asn Pro Arg Gly Leu Cys Pro Asn Val Leu Trp Gln Met Asp Val
      65              70              75              80
Met His Val Pro Ser Phe Gly Lys Leu Ser Phe Val His Val Thr Val
      85              90              95
Asp Thr Tyr Ser His Phe Ile Trp Ala Thr Cys Gln Thr Gly Glu Ser
      100             105             110
Thr Ser His Val Lys Arg His Leu Leu Ser Cys Phe Pro Val Met Gly
      115             120             125
Val Pro Glu Lys Val Lys Thr Asp Asn Gly Pro Gly Tyr Cys Ser Lys
      130             135             140
Ala Phe Gln Lys Phe Leu Asn Gln Trp Lys Ile Thr His Thr Ile Gly
      145             150             155             160
Ile Leu Tyr Asn Ser Gln Gly Gln Ala Ile Ile Glu Gly Thr Asn Arg
      165             170             175
Thr Leu Lys Ala Gln Leu Val Lys Gln Lys Lys Lys
      180             185

```

211

<210> 593
 <211> 271
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(271)
 <223> n = A,T,C or G

<400> 593
 actttatgtt cnagtgcana aancncctg gattgccacc ntactctcag ggctgtgant 60
 tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggg 120
 gtccctagct ggggtctata catgncnggg naagggcngc tgagtnccat nagcaaagga 180
 nctagnatnt gcgggggtgc ggcctgggcc taccctttna agcatcctn gatccactcc 240
 angaancng gggtagnacg gtttnccaac a 271

<210> 594
 <211> 376
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(376)
 <223> n = A,T,C or G

<400> 594
 cctttggggg nggggggaac ctttaccatt gtnccccttt atttcatttg gttnggggtc 60
 gcgccctcnn gggccaacaa agttatcgtn nttgaagaga anattttttt ggnttngncc 120
 cgattaagcg ncaaattgtgt agcaaaangc cgtgccactt gtggcgtagc tncgtcgggt 180
 cgattcgacg acaaggcgtn gcgcgntanc gttagtcten aatngaccn gtggcatgag 240
 cccacgangg nttcgtgtcg tcacatggnc tctagacata acgcnccn ttttttncag 300
 agggggntgc cgcccttagg gaggnagggg tggggacact agccaancca nantctnacc 360
 ccattgaaga aaaggn 376

<210> 595
 <211> 242
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(242)
 <223> n = A,T,C or G

<400> 595
 agnctgctgn tcgtnccctn tatgtggctt catnntgagg acaanagtng cactgaggct 60
 tgnngnatgcc aggcaaggnc aagctggctc aaaaagcatc caccacctc tgnaangggg 120
 atgccangag cangtgcacc agtcccaact angagnccn ggcattgntac atcttcttcc 180
 acccctnaaa ntttngcta caangnccat ttttctttt ctcttaaggg ncnctggct 240
 tc 242

<210> 596
 <211> 535
 <212> DNA
 <213> Homo sapien

212

<220>

<221> misc_feature

<222> (1)...(535)

<223> n = A,T,C or G

<400> 596

accagttgga	tactgctaaa	nagatattta	tcgagcctca	tatgttaagt	cgtatatttt	60
gaaagctttt	taaatttttt	ctttaagaag	attttagatg	cttatcactg	agtaccagag	120
ggatgtaggc	tgatgccctt	atcaacaaag	tcagggaactg	tggcacacaa	ggattgacta	180
ctgcagacac	ggccacaatg	ctacctctag	agggcctgaa	tccccctgcc	ctctctggtg	240
gggagaaggg	ctggcagagc	cattagcatg	ggctccggcc	aatcctggcc	actttgacac	300
tcctgggtgct	gacccagggt	cctggaggaa	gggatgaggt	gggcagtaga	gatgctcagg	360
gcagtggccc	ctttccatcc	acactggaac	tatttcagta	ttttaccacc	aattcagcca	420
ttcccttggtg	cgctggctga	acatcagccc	tgctccaggt	ctcagtttcc	cctttgtaaa	480
gggaaagctc	tggattcagg	gagtgatgaa	gagggtcatca	tggtcttgag	aattc	535

<210> 597

<211> 257

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(257)

<223> n = A,T,C or G

<400> 597

tttcnatacc	caaaantacc	ccatattang	accanacatt	tgtctnggaa	aaattaccat	60
tnntnaacnt	ttggggccacc	tgagannaaa	tggtgttaat	ncatgataag	atggancagn	120
attnctctta	agatnngatn	agaccccggt	tttcacggaa	catatccaag	nacccaatag	180
gnaacaagcc	acggngggag	tcacaaacat	atattcttta	ctctcataat	ccgtnnccaca	240
naactnttgn	acttgac					257

<210> 598

<211> 222

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(222)

<223> n = A,T,C or G

<400> 598

nntggntacc	gtcnaaactt	nncttggtac	ccgagctcgg	atccactagt	ccagtgtggt	60
ggaattccat	tgtgttgggc	tataagctgt	aatagtggag	ncgtgctngg	ttcattgcan	120
nagnccctcc	gcanncacnc	ttgnnacaac	ctgtgagnag	gcnataaatt	attcacataa	180
tcatcactgc	atgaanctga	ctcaaacgca	tccacntaca	cc		222

<210> 599

<211> 238

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(238)

213

<223> n = A,T,C or G

<400> 599'

gcatgacatc	ancgatgtnt	ttggnnacct	ganattngct	aaaactngng	natgccgggn	60
atgnaggttt	ggtantgatc	tatgactca	catctcatgg	ggacgtttca	tgtggagtgn	120
tcgacaangt	tgctgnancn	gagaagtgat	gatctcagtt	gaaaggggtca	tgtgaatata	180
cnttacactt	gaaaaagaag	cacattggga	atatcacgaa	acgnccacca	acatcctg	238

<210> 600

<211> 232

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(232)

<223> n = A,T,C or G

<400> 600

cgaactat	agactaccta	ggaaaattat	tttagtatca	gaagaatata	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatgttag	tttgtcttcc	gccatttcta	120
cagaaagctg	caatttcagg	ttttcaacct	aatagggtgat	atttaanaaa	aaaaaaaaagc	180
aatcgcaaat	agccccactg	cttttacaaa	tcattttttc	cccaacacaa	tg	232

<210> 601

<211> 547

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(547)

<223> n = A,T,C or G

<400> 601

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgagg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tgcagctttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatattag	ctctgatgag	tactacaccc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagtttag	taactcaaaa	cgagtgcata	tnggaagtat	cgagccggt	300
nctggatnaa	attcccagct	tgctngcttg	ctnagccggg	gggcggtnaa	aaaaacatct	360
gcagcccnng	gnaaaaaacc	ttcgcatgtg	tcttacgtgt	ttacgttatt	ttatttccct	420
nnagcaaggc	nggganttg	ggactcgaaa	tggtagagtt	gggctgggga	tcgcccttgt	480
tacataaaag	ncgtccagaa	gagggacggt	tacaggcnng	ganctccaaa	ggtcagtcct	540
tgccatt						547

<210> 602

<211> 826

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(826)

<223> n = A,T,C or G

<400> 602

cggggggnnt	tacgtctctc	tggacgcttt	tattgtacca	gggcgatccc	agcccaactg	60
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214

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taccattcga gtccctactc ctgccttgct ctagggaat aaaataacgt aaacacgtaa 120
gaacaatgcg aaagcgtttt cttccctagg ctgcagattg tcttcttcac cgcccctgct 180
tagctagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca 240
ctcgttttga gttacaaact ccgcggatta catgtctttt taaaaaagtt tagactacac 300
tagggaaaat tatttttagta tcagaagaat atcagggggg gtagtactca tcagagctna 360
atgagagcgc tttaaaaatg ttagtttgct ttccgccatt tctacagaaa gctgcaatth 420
caggttttca ncctaatagg tgatatntaa gaaaaaaaaa acaatcgcan atagcccact 480
gcttttacaa atcatttttc tcttctaggt atagcctgtc aggtggccta atgtattttt 540
gacatctcta ggaattttta tagaccagaa atgggtgccg gagatatgcc tgcactaatc 600
ttaagtgggg atttatgtat ttctcaanca agtgattaaa gcaaaactag gcacgaatga 660
aatcaagatc tttaggccag aaatcatgaa nanttttana attattttan gaatctgtgg 720
cttctcttct taaaatngaa aaaaaaattg tttaaacca naaggtctga ataccaagc 780
nccctgaacn anagaacaan gccggagcac cccctcccaa atcccc 826

```

```

<210> 603
<211> 817
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G

```

```

<400> 603
nnangacttt tgtggtntta tacaattntt ttttctattt ctatgaagag aaagccacag 60
agtcttaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120
tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt 180
agtgcaggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa 240
aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca 300
gtggggctat ttgcgattgc tttttttttt tcttaaatac cacctattag gttgaaaacc 360
tgaaattgca gctttctgta gaaatggcgg aagacaaact aacattttta aagcgctctc 420
atttagctct gatgagtact acaccctga tattctctcg ataactaaaat aattttccta 480
gtgtagtcta aactttttta aaaagacatg taatccgcgg agtttgtaac tcaaaacgag 540
tgcatctagg aggtatcgca agccgtttct ggattaaatt ccagctagc ttgcttgctt 600
agcagggggc ggnaaanaag acatctgcag cctagggag aaaaccttcc gcattgttct 660
tacgtgttta cgttatttta tttcctanaa caaggcngaa ttgggactcg aatggttcag 720
ttgggggtgg ggatcccctg gtncataaaa ngtcanaaag anggtacag cggaacncca 780
agggtcgtcc tgcatttana ctcggaattt tgggtgcc 817

```

```

<210> 604
<211> 694
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(694)
<223> n = A,T,C or G

```

```

<400> 604
cttttcaaat catttttnct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60
gacatctcta ngaattttta tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120
cttaagtggg gatattatga tttctcaagc aagtgtataa agcaaaacta ggcacgattg 180
aaatcaagat cttttaggca anaaagtcac gatgagtttt agaattattt taggactctg 240
tggtctttct ttcatagaaa tagaaaaaaa aattgtataa aaccacaaa ggtcctgaat 300
agccaaagca acactganca aaaagaacan agcagggag caacacacta ccngaattca 360
aattatacta ccagggtgta gtaacaaaaa cagcattcta ttggcataaa atagacacca 420

```

215

```

agaccaatgg ancagaataa agaacccccc aaataaatcc atatatntac cgccanctga 480
ttatcaataa cnaacaccaa gaacatatnt taagggacnt nctattcaat aantagtgt 540
ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agaccocctat ccctcaccat 600
acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660
atnaaancta ctattaagaa aacagatcnc nccc 694

```

```

<210> 605
<211> 678
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

```

```

<400> 605
taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttaa aaatgttagt ttgtcttccg ccatttctac 120
agaagctgc aatttcagggt tttcaaccta ataggtgata tttagaaaa aaaaaagca 180
atcgcaata gccccactgc tttacaaat cttttttct cttctaggta tagcctgtca 240
ggtggcctaa tgtaattttt gacatctcta ggaattttaa tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa 360
agcaaaaact ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt 420
anaattatth taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaataaat 660
cctatatatta cngcccncc 678

```

```

<210> 606
<211> 263
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(263)
<223> n = A,T,C or G

```

```

<400> 606
gtgggggtcng cancagccaa ctcagcttcc tttcgggctt tgtagcaga cggatcatcc 60
tctagtcac tgtgntcaaa ttccattgtg tgggggccnc tcgcctcggc canagatctg 120
agtgancana cntgtcccca ctgaggtgcc ccacagcngn ttgtnttcag cangggctna 180
caactcgacc ggcagcgnan ggctggcaga antgngcgcc tnnctcattc ctacgcngtn 240
ngccgcagga aggangacag gcc 263

```

```

<210> 607
<211> 22
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> Primer

```

```

<400> 607
ccatgtgggt cccggttgct tt 22

```


216

<210> 608
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 608
gataggggtg ctcaggggtt gg 22

<210> 609
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 609
gctggacagg gggcaaaagc tggggcagtg aaccatgtgc 40

<210> 610
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 610
ccttgtccag atagcccagt agctgac 27

<210> 611
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 611
gatagagaaa accgtccagg ccagtattgt gggaggctgg gagtgc 46

<210> 612
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 612
gcacatgggt cactgccccca gcttttgccc cctgtccagc 40

<210> 613
<211> 38
<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 613

gccgctcgag ttagaattcg gggttggcca cgatggtg

38

<210> 614

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 614

cggcgggcat atgcatcacc atcaccatca catcataaac ggcgaggact gca

53

<210> 615

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 615

gcactccag cctccacaa tactggcctg gacggttttc tctatc

46

<210> 616

<211> 1350

<212> DNA

<213> Homo sapien

<400> 616

atgcatcacc atcaccatca catcataaac ggcgaggact gcagcccga ctcgcagccc	60
tggcaggcgg cactgggtcat ggaaaacgaa ttgttctgct cgggcgtcct ggtgcatccg	120
cagtgggtgc tgcagccgc acaactgtttc cagaactcct acaccatcgg gctgggcctg	180
cacagtcttg agccgacca agagccagg agccagatgg tggaggccag cctctccgta	240
cggcacccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac	300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc	360
gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc	420
gtgctgcagt gcgtgaacgt gtcgggtggtg tctgaggagg tctgcagtaa gctctatgac	480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc	540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc	600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc	660
actgagtgga tagagaaaac cgtccaggcc agtattgtgg gaggctggga gtgcgagaag	720
cattcccaac cctggcagggt gcttgtggcc tctcgtggca gggcagctcg cggcgggtgt	780
ctgggtgacc cccagtgggt cctcacagct gccactgca tcaggaacaa aagcgtgatc	840
ttgctgggtc ggcacagcct gtttcatcct gaagacacag gccaggatt tcaggtcagc	900
cacagcttcc cacaccgct ctacgatatg agcctcctga agaatcgatt cctcaggcca	960
ggtgatgact ccagccacga cctcatgctg ctccgcctgt cagagcctgc cgagctcacg	1020
gatgctgtga aggtcatgga cctgcccacc caggagccag cactggggac caccgtgtac	1080
gcctcaggct ggggcagcat tgaaccagag gagtctctga ccccaaagaa acttcagtgt	1140
gtggacctcc atgttatttc caatgacgtg tgtgcgcaag ttcacctca gaaggtgacc	1200
aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa gctggggcag tgaacctgt	1260
gccctgcccg aaaggccttc cctgtacacc aaggtggtgc attaccggaa gtggatcaag	1320

218

gacaccatcg tggccaaccc cgaattctaa

1350

<210> 617

<211> 449

<212> PRT

<213> Homo sapien

<400> 617

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Met His His His His His His Ile Ile Asn Gly Glu Asp Cys Ser Pro
 1          5          10          15
His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe
          20          25          30
Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
          35          40          45
Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu
          50          55          60
Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu Ser Val
65          70          75          80
Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu
          85          90          95
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile
          100          105          110
Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu Val Ser
          115          120          125
Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys
          130          135          140
Val Asn Val Ser Val Val Ser Glu Glu Val Cys Ser Lys Leu Tyr Asp
145          150          155          160
Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln
          165          170          175
Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly
          180          185          190
Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala Pro Cys Gly Gln Val
          195          200          205
Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Glu Trp Ile
          210          215          220
Glu Lys Thr Val Gln Ala Ser Ile Val Gly Gly Trp Glu Cys Glu Lys
225          230          235          240
His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala Val
          245          250          255
Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala His
          260          265          270
Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu Phe
          275          280          285
His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe Pro
          290          295          300
His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg Pro
305          310          315          320
Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu Pro
          325          330          335
Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln Glu
          340          345          350
Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile Glu
          355          360          365
Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His
          370          375          380
Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr
385          390          395          400

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219

Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Trp Gly
 405 410 415
 Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val
 420 425 430
 Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro Glu
 435 440 445
 Phe

<210> 618

<211> 385

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(385)

<223> n = A,T,C or G

<400> 618

ctgtgctgag	aacccaaaagc	tatgancact	gcttttccaa	atgtccataa	naccaacatt	60
tttatcacta	ccaccatcac	ctgggagctc	nttagaaagc	tagtctcccg	ggcaccaccc	120
tggcctactg	aacctaatgt	gcatttaaca	agattnacgt	ngaaatctgc	aaagcacagg	180
ggcngataac	agtaccacct	gntctgggtc	ctanccccan	gacccttaca	gtctaactgg	240
gacacaaggg	cttnaaatca	aattgcctat	cattaagata	tacaanganc	ntgagaaact	300
gctncactta	tntattaagg	ngctctaaga	cttagaaacn	aaangcantg	ctgagangat	360
tcaaatatga	ngggggncac	tttnc				385

<210> 619

<211> 869

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(869)

<223> n = A,T,C or G

<400> 619

gatatcccg	gaattcgcg	ccgcgtcgac	ctctacttgt	ttagacataa	atgcagtcta	60
gcattaaaga	tcctttaaaa	aaatgttttc	ccaatgggta	aaagacaagc	tcaataaat	120
gaactctcat	acatatgcca	aaattgatga	gtagataaat	atttcagtag	gtagttacta	180
gctttctgtg	tatgagtaaa	catatgggag	aaatttaaaa	cactaaagta	gactcaatga	240
aagcatagta	tcctatgtat	tcgtttttca	gaaatgtcta	atgaagggaag	gaaacaatga	300
atgaatgccc	ttattcctct	tagagtgtctg	ggacatgggt	ttgcctgaaa	acttcatgtg	360
aattttatat	tttgctacac	attacacca	tcttagactt	atagctataa	gacataaggc	420
atatcttatg	tcttaccatgt	ataataatct	aagcagaaca	aaaaataacg	aaatatattc	480
ttccccaaat	ttttgagaca	gatggatttt	ccggaagat	gtgttttagct	tttaatcctg	540
tggttttgtg	taccaccttg	cacactagag	tggtgtctcta	attcagtgag	ttgtaactct	600
gggtgaacag	tggaataact	agggtacatt	ttaaaaatgc	taatgctcgg	gcctcgctga	660
agaccaaaatt	aattgggaatc	tctgngggng	gnattgatct	ttttataatc	tttctanang	720
attctaattgg	gcttccaggg	atgaaaaccn	ctgntggagc	tnggaacctt	cctttagttt	780
ggagaaaccc	cgatgaggg	ntnttaggcn	ccgcctnttt	ttggcctggg	cttccccctt	840
tatntntntt	tgggaangnc	cnaattttt				869

<210> 620

<211> 339

<212> DNA

220

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(339)

<223> n = A,T,C or G

<400> 620

gngcgggcct cncctgtgctt gctctcgtcg cgcagcgtct ttttccacca gctgtaggan	60
aagcccgaag accactgggc ccccggttag cccaagtacc actggctctc ctggctctcg	120
acgctncggg tcttcctcgt ggcgtagact gccagcttcg gagacccctc agccctccc	180
cgcttttctc caccacagga ggccatcagt agcgagctac tgctcggcc acaacctccc	240
agcangatag cccgcgggtt ccaatctcg aaaggaggac cgccnagccc gaaatgccna	300
gccagcnat cactgccacg ccgagccnag cgctcgtgc	339

<210> 621

<211> 267

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(267)

<223> n = A,T,C or G

<400> 621

gggngcatg gtccnnggta gccaggtaca tggctcctct ggctcctgac gctacgggtc	60
ttcctcgtgg cgtagactgc cagcttcgga gaccctcag cccctcccag cttttctcca	120
ccccaggagg ccatcagtag cgagctactg cctcggccac aacctcccag caggatngcc	180
cgcggtttcc aatctgcgaa aggaggaccg ccnagccaga aatgccnagc cnagcgatca	240
ctgccacgcc nagccnagcg ctctgtgc	267

<210> 622

<211> 847

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(847)

<223> n = A,T,C or G

<400> 622

cttangntgt cgactgacgt catgcatgan tttaaagcaga gggttggtga aatttatgaa	60
aaatacaaaa ttccggcttg tcctgaggaa gagccactac ttgataactc tacaagagga	120
acagatgtga aggatattcc ctttaatttg acaataaaca tacctggttg tgaggaagaa	180
gatgcatctg aaatatctgt ctcaagtgtg ttcgagacat ttctgaaca aaaagaaccc	240
agtctcaaaa atatcatcca tccatactat catccgtact ctgggtccca ggaacatgtt	300
tgccagtcac cttctaagct tcattttacat gaaaataaat tagactgcga caatgataac	360
aaactaggca ttggacatat ttttagtaca gataacaact ttcataatga tgcaagcact	420
aagaaagcaa ggaaccacga agtggttacg gttgaaatga aagaagacca agagtgtgat	480
ttgcaaatga caaaaaatat gaaccaaaat agtgacagtg gcagtacaaa taactataaa	540
agcctgaaac cttaaattaga aaatctgagt tctttaccac cagattctga cagaacatca	600
ggaagtatat ctacatgaag aattacagca agacatgcca aaagttaaag aatgangtca	660
acacattaga aanaagantt ctgggctttg aagaaagaaa atgttccact tcataaagaa	720
ggttgaaaga agaattggag agccnngaan tttttgccn gaaattttcg ggaaccctac	780
tgatgggtc nactggttgg ccatgaatga ataattgact aatcnnccaa ttcctnggga	840
agggaat	847

221

<210> 623
 <211> 681
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(681)
 <223> n = A,T,C or G

<400> 623
 aaaactgtac tcgcgcgctg catgtcgaca ctagtggatc caaagaatcg gcacgagcga 60
 aaangctcan gcagcccgcc tggecgccgc cgctcctccc cccaggaaag ccaangtgga 120
 ngctgatgtg gctgcangag ctctgtttcac agccctcan gtgganctgg ttgggccgcg 180
 gctgccangg gcggaagtgg gtgtccccc cangtcagccc caaggctgcc cctcacaaaag 240
 cactggtggt ttgcctccac tgccaccttg ggctccgaac ccgctcccct gctgtggang 300
 cccaccgtgg gaatccaggt cccaggtgg actgcctgcc ttgcctcac tgccactct 360
 gccacactt ccctgcctag anaccgggaa ggggctgtgt cggtantggt gccaccttg 420
 atgtggcagc accgactgtg ggggtggacc tggccttgcc ggggtgcaaaa gtgggggccc 480
 ngggaaaaag acctgaagtg gccctgaaaa atccccctt aatttttccc caatttgagg 540
 ctcaacaaa aggaattgc tgaagccaan ggtaccaagg tccccctaa ggccagggtg 600
 aaaaggtccc aaaattccaa tnccacnt ttgggcttnc ctcttgaac cccggccccc 660
 tctcntgaan ttttaaaaaa n 681

<210> 624
 <211> 661
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(661)
 <223> n = A,T,C or G

<400> 624
 attggtctta ctgtaccacc ggggtgaaat cgatggccgc ggcgtctaaa tatccgattt 60
 tttttttttt tctcttctg actgtccatg gacaaatgaa actaacttaa tctaactaaa 120
 aaacacaact atattttgaa gattttctat ctgcactcaa ggacactttc cacnccggtg 180
 ttgttacctt ttggtcttgt ctctgaacat gaaattnatc tcaagggatt ngatttctgg 240
 acctcctatt cctgctatgg gtttgatatt tcttgggctc cagggccact gttgcattgg 300
 gntgacagnt acctcctagc ccatancctc ctatcttggg aaacaaacct aacaactacg 360
 tgtaccttcc atagatctct gattgagtct cagtatncgc ttgctcatgg gcgattcact 420
 tgaatccgtn attggtgcca acaatcctga ctcatgggnn aatggatcct atcacgttcc 480
 cctgattngc aaccctgtg tacatanatc taatcgcatg gaactctagn tnggntatgc 540
 gcggctacgc tatcagggtg tgntaactat ngcatggcta cgaancctga tcatgatcna 600
 gggctatgga ctcttatcag ggggggttggg ccngcttct ttttcnnacc ttggtaaaac 660
 c 661

<210> 625
 <211> 181
 <212> DNA
 <213> Homo sapien

<400> 625
 gcaacaatca gatcatgtta aagtaaatct ccattgccct ggatcacttc aggatttaat 60
 tgtccaagga gagcagggtt ctctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa 120
 aatacaaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataaag 180

222

c 181

<210> 626
 <211> 181
 <212> DNA
 <213> Homo sapien

<400> 626
 gcaacaatca gatcatgta aagtaaatct ccattgccct ggatcacttc aggatttaat 60
 tgtccaagga gagcagggtt ctcctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa 120
 aatacaaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataaagc 180
 c 181

<210> 627
 <211> 813
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(813)
 <223> n = A,T,C or G

<400> 627
 accaagctgg agctcgcgcg cctgcaggtc gacactagtg gatccaaagt gaacgtgaag 60
 gtgagcagag gagaacttgc gatggcaaag ttaaaaacaa gaggagatga tgggtcttgg 120
 gtggcacagg atgttaaaaa aattctcctg tccttaagga gttactgcta tttgagtaat 180
 gtgccacttc cctacatagc cttctatgca gaaatgctat atttccactt cacaaccag 240
 aacgtgcatt ttatttttaca tttagaggag gaacaaacaa ccagaaggca aaaactgg 300
 cattatTTTT tgcaattctc ttggaaagag ttcgTTTTta acttctgctc agacagcaca 360
 caactactgg gaatatattt taatttcaaa tctgatgtgt gacatctggg aactcattta 420
 ttgctaataga agttttcaca ggaagcagca gtcaccagta gctcatctta tttttcagtt 480
 ggcaaagtgt tgtttacctt ttattggcct gcacgggtgt ctcttatcac aggatattta 540
 attagaaaac gcaagtagcc taacatagaa nagaaatggg gtggtagata atagtagata 600
 gaatgggctaa atatttttat tacagtgtat taatatcact gnaattttatg gttaaaaatt 660
 atgtaatact caaaaggaat tctcagactg gcgaaacagc tggnaacag cnttcacagg 720
 gctttnanct cctnttgagc tttccccctg ntggacttta gtcttcttt tacnccccgna 780
 gtnccattn nttaccaatt gtnccgggaa ana 813

<210> 628
 <211> 646
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(646)
 <223> n = A,T,C or G

<400> 628
 tttgggnggn ggtgtctcnt ttgggtggac tttttgggtc gtagggcccc aaggccgtta 60
 atcccgtaat aacggaagac gaagaagagt cagaagagtg cttctataag gatcgggacg 120
 agactacctt agaggaataa aggaaaaaag cagaggagga agagtggtag aaggagtcag 180
 aagaaaccca cactcgcttc tgaacctgga gccttatcaa aaaggctctag ataaacgata 240
 gcgatctcga tatcgagctc aagaggtagg ttttagagact tctcgctctc gagagcgaaa 300
 tggaaagatc cgacgacgat aagaagttaa agtgtagagg gtgcttgagg agcgcggtga 360
 aggatctctg cgagggaccc atcgacgtag agacttgaag gcctactaag gtccacaaga 420
 agcccggtc tttctccgaa tggtcggagc gtacagtatg cgacgtcgat cggcagacaa 480

223

gctggcggtg	gactcgaagt	gttcggggcg	atcgacttat	aatagtcgcg	cgctagtaac	540
gtaggaacac	gaagagtagt	cgaaagaaaa	cgtttagtga	gggaaaagat	tagggaaaaa	600
ggagaggcct	aataactaag	acacttggag	cctaggccaa	cgcgaa		646

<210> 629

<211> 617

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(617)

<223> n = A,T,C or G

<400> 629

gccccnccc	ccctcctngg	gcttatnggg	acagaccac	gtagtactct	aaatcttctc	60
ctacgccgga	caacggaccc	tataccaatt	cgaatcttgg	acactccgac	cgccggattc	120
tcttccccct	tcggcttccc	ctttctgtcg	gtacccctcc	ctagtctctc	cctacacctt	180
cgtaaccgtc	atatatagtc	gccgaggact	agcctattta	ggtgtcctag	actcgttatt	240
gateccactc	ttagtctagt	actatgcgtc	acgtatctta	gttgcctaag	agggagatta	300
aatcctccac	aagtcccgac	gaattcctgg	actctcgtac	tagcaaaact	tcttatgagg	360
cttccttcta	tatcttctgg	atgtttctcg	tgtcccggtc	ctccgctact	actagagctc	420
cttgccctat	ctctagaagt	agaggactct	cgggttcggt	ctccaaatct	agcgctagag	480
ctatcgctac	ccgctcgatt	ccccagcg	aatcttgaaa	cctgaggtag	tacacaaacc	540
ctccnctat	tccctcggtt	gtccttctt	ctcatcccc	cttccgcct	tctcggaan	600
gaatctactt	tanccttc					617

<210> 630

<211> 644

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(644)

<223> n = A,T,C or G

<400> 630

cnntcggcnt	gggttttntt	ctgagnnncc	cccccccccc	cccccccaa	cttacacca	60
caaaacactt	tcgccccct	acctaggaga	cattagaagg	gtttaggctt	cggcgtatag	120
taaagtcctc	tacctcgga	gtagagaatt	cggtatttaa	attcagggtt	agaggctcgc	180
tcgttagatt	tatagtttag	gtttagaatc	ggaacccttc	gatcttcctt	agaagggtaa	240
taagtgaggc	cctaaatccg	tctaaccaag	gcgttaaggt	ccgtacctaa	acctagtctt	300
atcttctatc	aggcgaccca	atataggtag	gttctacttt	cgtataggcc	ttaaggaata	360
gttcggtagt	tatcgaaggc	actcctctct	aggctaggct	tttctcagtc	ttagtactcc	420
gggaccgtcg	tcgcanaaat	atcgatggac	ggtaggtatc	tccgcgttac	gcgtcgggct	480
agggatatag	agcgaattat	cggcgagagg	cggctcgctan	gaatcggtat	caatatgntg	540
ttctttacc	tacggatatc	ggcagaaaac	ataaacctt	ctnaccangg	ataagggtat	600
atcggacccc	taaaataaca	gtaacattta	gantactagt	accc		644

<210> 631

<211> 526

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(526)

224

<223> n = A,T,C or G

<400> 631

ccntcgggctt	gggttttttt	ctgagccccc	ccccccccc	ccccccccc	cccccccggc	60
cccatagccc	caccggnccc	acccaaattt	taacaaaata	aatntaccta	tcgntcacct	120
atcccnegta	tcgngtaggt	cggtaccggt	accgngatc	ncnacgattn	ttcgggtcgt	180
cnccttaan	acggncccgt	agccnccgga	anaaatacta	cgagngactc	taatntagca	240
anaccgcgcg	tonattanta	gcataccttag	tcttccaatg	ncgnggattn	ngaataccttn	300
naagttatcg	ggtagaacgg	gtcccgggtcc	cccgccctct	ttncaatata	cgccgggtac	360
aaantcgggt	tctaaattcc	ncacgaattt	ngncggcaac	attcncgggn	ccttattanc	420
cnthtccaac	cccgaacnc	nagctcgatc	gggctttanc	gaatccgggg	tcnccccga	480
ngantccggg	tcctttgagt	ngctctagga	cggttacgac	ggagga		526

<210> 632

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(647)

<223> n = A,T,C or G

<400> 632

tttggngggc	ggngtctcat	ttgggtggac	tttttgggtc	gtaggaacct	ggtatgaggg	60
gtgtttttag	tttcttcttc	gtcgtctctg	ggaggttcgg	tttcgattga	gattcgggtt	120
cgtctttatc	ttacgaggca	ccctgatatt	gttgcgcttt	ggtttgggtg	tggagagttt	180
tgtcctactc	tagcgggtca	tgcggatgat	atgtagcctg	cgtggcctga	tagtgatgtt	240
gtgagcttga	gaggggagtt	gtgggtgttg	cgggcggagt	aggaggggtt	ggagcaccgg	300
gattgggaga	tatagaatca	taagtgttag	gtataggctc	attgagcgag	ttcgtggaat	360
tcgtgtggtc	atcataatta	gagtgaggat	gggctctata	tttcttagag	gacgcacggt	420
cgtgattcgg	ggtttgatgg	gtgttcttct	tgtgggcacg	attagcttgt	tcattgatgtt	480
aaggaccata	ctgtttcgaa	tgaggattcg	tgtcttcgga	ttgttgttga	tattgtggnc	540
tanactatth	agtgttaagc	ggaggtgtgt	tgcctgtgtg	gagtatccga	nnttcattcg	600
ganggtatgc	gtgcggagcg	gtcctttagt	acattccgga	aaaatgg		647

<210> 633

<211> 630

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(630)

<223> n = A,T,C or G

<400> 633

tccttcggct	tgggtttttt	tctgaccccc	ccccccccc	ccccctcgga	aggcctctag	60
gtctccaccc	gtctctctaa	tcctcaggaa	ccgatccacc	caaccaactt	actaatgtcc	120
tacagtaaac	acccgagaat	ataaaccac	acctaggcct	ccaatcctac	caggaagca	180
agaagccgta	gtctagcgta	ttacgaaccc	gagatagaga	cggagatact	tagttttatt	240
ctctcggaat	aggaaagacg	actggggagg	gaatatagga	tagcgcgggg	ataggggcta	300
tggcggatat	ggggcggggt	cgctctctta	ttcttctata	ccacgtcaat	aggaatgtag	360
atatacctag	atgttcccgt	agaaagagac	gttagaggtc	tcgaagcta	taaaggagag	420
gcgcgaagaa	acttcgtact	ctagctttat	ataggtagtc	gctctagtcc	cataagcgac	480
gagagatcta	ctagatttcg	gtatcgccgt	cgtatgtatt	cgaaatagtc	ttcttcccct	540
tttcgatctc	ctctctatac	tacatggnga	ttatagtctt	aagatagtc	ggatattagg	600
atattagtta	tatgacgttc	gacgggacgg				630

225

<210> 634
 <211> 647
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(647)
 <223> n = A,T,C or G

<400> 634
 ccntcggctt gggttttttt ctgaaccccc ccccccccc cctccactaa gancttaacc 60
 caaccctata gtttactcgt ataggggaat cgaggagaaa taggaacgaa gagcgggtga 120
 taaagagaaa gtactttcct ttatatgtta agagcttagc gtaatgactt tcgttatatg 180
 gctagttgat tttatccggc gttatagggc ttagttctgg ttatctcggg tctaattccc 240
 ttagtatgct cgggagttta acgagggtcac gggatagcgc gtaccctttc taaggttcct 300
 ggaaagctat tcgttattta tcgcgattct cgaggtcgaa aggatcaagg atcttccctt 360
 ttactaccct agtcgggtta gcggtcggtc aaaactagt tagtaccttt acctcctcga 420
 aagttatagt cgaaacaacg tattagtcga aattatagcg gatagatcga gacggttctt 480
 tctcgggttc tcagccggta atccctctat ttgggggtct tctccctctt cccctttgtc 540
 ttccgcctta gcttccaagg ttccctcgga gcgaggggtt ctacttaagt cgntagcggt 600
 ccttataaac cncctacagg cagaccccc tgtaaacggc tcggggt 647

<210> 635
 <211> 645
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(645)
 <223> n = A,T,C or G

<400> 635
 ccttcggctt gggttttttt ctgagcccc ccccccccc cccgaaactc gccttaccct 60
 agatacccaa agaatagttc cactcaactt cgtctaagta aaactctaga acttccaaac 120
 ataaaagact tcgctcgggt agctacacag cctacgggaa tctcacgaat cccgattcaa 180
 gtcccactct cgaccacacc ccggtatcgt cgttttccca taccaatgtc gaaaaataaa 240
 ataaaatcca gtcaagcccc acggttaagc ggggtagggc taggcgaaga ggcaggaacc 300
 gtctgaggcc gggggttttc aaaatacaaa acaactactt aaagtttacc ccttctaaag 360
 tcgggggcaa cggttaaagc acgcctctaa agtactactc gtttcgagaa ggggtagtca 420
 tctcccgcat agagactctc gcgtatatca actcgcatcg cttctagcat tccgacggtc 480
 gcccgcggt acatatcttg cggattagct ccgagggact atagggttaa ttagtctagt 540
 aaattctctt agaggatagt cggggtcgta gttaggcagt acgaggggac atggnctgag 600
 tcgtgctcta ccttgacagc atactcttat aaacatcttt ttctt 645

<210> 636
 <211> 643
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(643)
 <223> n = A,T,C or G

<400> 636

226

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ccttcggctt gggttttttt ctgaccccc ccccccccc cctagcgga aacaatcccc 60
accgagattt tattaatcgt aaaactcgcc ttcggtacca agtcttcctc cttcccgtaa 120
cctggctccc tcctagnngc tttacgaacg tccctcctct tcttacggct cggaagtgg 180
tacggttaaa tccggaggng gggctaacga atccaaggct aactcctctt anagtgtgt 240
gtccncncgt ttagtaagga tccgtggagg gcgagtattt gnccccggc ctttatnta 300
tagttcccta gtacgataaa gntaccggct atcctattac agcggataaa agttatttan 360
agggccgacg tcnccgctag acaggctaca gctagnggag gtaccgcctc cgactantcc 420
gttgnttcg acaaggnagt ttcggttaac tccacaaact cctccgccga ctctanggtg 480
gggacggcag ttccncngtt tagtgtgcgt tatagagaag ggcatttgag ttggacgtta 540
cnttttaaca taggttattc cgttttaggt cttgcgggcc cgtgggggta gtncnccggc 600
gcgttnntat cggcgatttt ccgcagtttc cgtttccggn tnt 643

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<210> 637

<211> 631

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(631)

<223> n = A,T,C or G

<400> 637

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gggttntctc atttggttg actttttggg tcgtaggaac cggtatgnag gagtaggagt 60
cgctgggaag actagaagtt agctacggac gattagtgtg attccactct taataacgag 120
taatcgttta cgctcgggtt gtgtttcggg gttttggaga gtaagcgtag ttgtggagt 180
tcgcatatag gtccctttac ttcggcgatc tcgtcttctg tcggttaggt tattattgt 240
catccttcgc attagtagta gggttggtcg gataaatcga tagctattct ttagaattcg 300
tagtcggaga attcgtgtac gaagtccttt aagttcttta agttcgcgag taagacgtgt 360
acggttattt tgtcgtcgac gtaggtgtcg ttacgggag ttctgtttta ggggtttacg 420
tagaacgtta ttaagcacgg taatacgata gaggattacg cgacgtattc gtcttagaac 480
gtcgattttt cgaaggcgca ttgtttatcg aaggggagtc cttggagaat cgagatattc 540
caagaatatt acgagatta cagatcggaa ggctcccag atcggacgta ttaccggtct 600
cgcccgaac gagtaggtat cntccgata a 631

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<210> 638

<211> 606

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(606)

<223> n = A,T,C or G

<400> 638

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ccccccccc ctcaaccatc nattccccac ctcaacgcga attacggttt cgaaagtcga 60
caataagtcc ggtcgagtag agggaaatcag gggctggtan aaaggaccac gggcggaaaa 120
taccggtctc cttccgggga gcgacgtcgg ggaagggaag gagagcggtc tagttcgtag 180
gcaaacaggt cagaaaagtt aagggttaaag gtcggagggg agaggatagc tagtacgctt 240
agttcggggc tcgggcgcag ggccactttc ctctttcgcg ttctttact ctgcttacga 300
gttcaggctc cggagttccg cgccggaggt cgtcgcgacg ctaggaatgg ggactcgctc 360
agtccccggt tatccttcgg gattctatgt ttccgccgat agacggagac cgggtagtag 420
ggttcgctcg taccgccact cgtcgccttg atccggcccg ctccgcttaa gggcgatgaa 480
agattaggtta ttagggctct acgggacgag gcatagggcg ggagaagggg ggaggggtcg 540
ggggtcgaag ggantaagaa atcgcantcg cgcggggtcg gtagganccg aaatttttct 600
cnnctg 606

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227

<210> 639
<211> 592
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(592)
<223> n = A,T,C or G

<400> 639
tcntcggct tgggtttttt tctgagcccc cccccccccc cccccgggaa cgagaaaaca 60
atcccaccct accgcgggga gtgggttgna cgcttagttc tagaatcctc ggaatcgtcc 120
tcgggcgttg gtagttccgg cgattccgag tatgccgaag tgtatcgctc cgtctagagg 180
ttggtatctg tttatcgcca tgacgctatt gactcggatg ctttcgaagt agggggatag 240
gcgcatagat acgcctccgc ggtgtcctct gaagtggcgc catccgtgga cgcagcgtag 300
acagctcttg tggacgataa cggcttctcg tactcctact ccggctatta tgtagagag 360
gacttgtttc tgaacggata taccattagc gaaggggtac cctccgctaa cgcaggcgtt 420
tctaacagtt cttccgggcg ctccgaattt agattgacgc ctccgcagca ttgtgggac 480
ctcttccgtt agccctcttt ataggatttc tcctccgccc cgaaagangg ctggtcgtcc 540
ccggcangta tgtctagctc gaacgctttg ttactccttt gttttcgaaa na 592

<210> 640
<211> 637
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(637)
<223> n = A,T,C or G

<400> 640
ctttgtggcg gtgntgtct catttggtg gactttttgg gtcgtaggct tatccgggtt 60
gggctcccga agtagcttag gatcgccggc tagttccggt cccgcccgtc gaaagcgcgg 120
ttcggcgggc ggcccgcgt tcgttcgcgg gctttaccct catagagtgc caggctcgcg 180
ttcttacggg ttcgtcggcg atagatttta cggcgagagg tcggatatct cgcgcgttta 240
cgttcggtcg gcctctacgc ctagtccaca ggtagtttat gcgccggagc gcgtgacgga 300
gaggtttatac gggacgcgga agaaccgcct ccaaatgact agtacaggct cgttcgggcg 360
tagatctcct cgctcggtcg gcggttctta cttctagggc cgctctacgg tttaaggcgg 420
tcgttagatc ttagaaacta tactcaagtt tcagtcggaa gaaaggaagt agagagaagg 480
gtaaacgatt acctccggtt ctageccctt ttactcgcat aacgggagaa cggggtccgg 540
ctctcagata cgctcgcga gacgtcgcga ttcaacttta acctccgcta gggcatccgt 600
atacggttaa cgcggtaaaa gcgacctcgg aaacctc 637

<210> 641
<211> 649
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(649)
<223> n = A,T,C or G

<400> 641
ctntgtggcg gtggttgtct cagtttgggt ggatttttgg gtcgtaggna acctggtatg 60
aggctagttt tcttcaacga ttcttggttc agttacgcga ccctatcctt atcttacaat 120

228

gtcttctaca	tcaggttcat	caattaatat	atcaattaca	cattaacgac	ggtgtgacgc	180
aatatgagaa	agtatacatt	aaggttatta	tatattattc	gcttaaaaag	gttcctgaca	240
tgggacaact	tcaccaccca	ttctagaagc	ccccctcct	gtaggacccc	ctcgagttcc	300
ccattatctt	agttcagttt	tcatttttta	accaggaggg	tatcggtttt	taataggtag	360
tattttgtca	aacttttcag	aagctttatc	ttcaaatata	cttgaccat	ctgtactagg	420
agcactaact	attcgagtct	attacagctc	aacagaaaat	aattgaaatt	aaacaacctc	480
agtatcgctc	accataaacc	catcgggctc	tcacccatt	tcttcataag	ttctagagca	540
tcctgagctc	tttctatta	cccttgatgg	tactcatggg	ctaatacccc	ccgcagttat	600
aggtccttat	ggatcctatg	ctaccaccgg	tctaatacct	tctatcacn		649

<210> 642

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(645)

<223> n = A,T,C or G

<400> 642

tccttcggct	tggtttttt	ttcgctcgcg	gttactatta	tcgattgtta	cttgtaaagg	60
cgatactccc	accgctcacg	atattagacc	tgctcctcta	gaagcgaacg	gcgataggtc	120
tactcgcccg	gcgaagacgg	cgaacgggta	ggaggagcca	tatgcaaccc	taacggagat	180
tataagtact	gggaaaaata	ctagtattaa	ggtagcgggt	taagatagg	ggagagacac	240
tattcacgag	cataagcact	tagaaggctc	tctcgaggag	aggtaggcta	cggactacgt	300
tccttctctc	tctagcctcg	agagggagta	tagatgatcc	gcaaaagaga	atccctccta	360
tacgctggca	taactagacg	acgcgtcgct	gggaaatctc	gccaaacctc	ttgcgacctc	420
caaaaggaag	attgtcgttt	catagaacgc	taatactccg	ggtcttcccg	aatcatagcc	480
gcataatcggt	aagaagacgg	taaaatcgcg	cgattctaac	aagattctgt	agacttaagg	540
ctaagcacta	gaagcgatct	cgattccgga	tcttaagatc	ataactaatag	ttcggtcaca	600
ccagacgacg	attagccact	agaagcccta	ctccgtnгаа	accgg		645

<210> 643

<211> 586

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(586)

<223> n = A,T,C or G

<400> 643

ctttgtggcg	gcggtgtctc	atttgggtgg	atttttgggt	cgtaggaacc	tggtatgcag	60
ggtccgcccc	gaattaaaag	cgggatcccc	aaaacgnngn	ttcgcaagaa	gagaagaatc	120
atagcgatag	anccttcata	gtacaaaggt	aactaagagg	aaaataatgc	agattcagaa	180
ctagttgccca	aattagaact	cgattaggcc	aaggatccga	gcctggcgct	atcacttcgg	240
gacttaagct	acggtagagc	agtcggtcct	gaagcatagc	tcccgtagga	cgtaggaaac	300
tagtccggca	cggaggacat	actctcgagt	ctcggaacgt	ctatttagaa	tataaacgca	360
ttaacctcag	aaggcgccga	cgcggttact	ctctagggaa	ctatttcatt	ccttcggag	420
ctcccctatt	tttccaacac	atataccggc	aaaggaaaat	cttntgtcct	cgggtctaaag	480
agagggaaaa	aaaacgatat	ctaggttcgg	gtttatccat	ttaaaaaanat	ngacgcgact	540
actccctttc	aaaggagatt	tccccctagg	nagagttcaa	cnгаа		586

<210> 644

<211> 646

<212> DNA

229

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 644

ctttgtggcg	gtggttgtct	catttgggtg	gcatttttgg	gtcgtaggaa	cctggtatng	60
agggtctattt	gacttgtttc	tcaaatccca	tggtatggtg	ggtggcgtgc	ggggtggcgg	120
tcggttcggc	gggggtgggg	gtcgtcctcc	aaaggagttg	ctagagggct	tttagtggtt	180
ttagggcggg	aagggttag	agcggagaga	cgtcgtcgtg	gaagcttctg	gcggagcgcg	240
agaaggtagt	tagcgccggt	tcggaagatt	ctcagaattc	gagaagaggt	agtggggcgc	300
ggagagagag	tttctaagtc	taaacgtaga	ggtcgtccta	gtcgggccgg	gagtagcttt	360
taagctagag	gtcagagtc	tcgttttagc	tccgggctct	tcgggcagta	tcctctttct	420
cagagAACG	agcgaccgac	gtcgtagccg	gacccgtcta	tccgtacgtt	tagagatacg	480
ctcacctcca	cgggcgtata	tgcccgtata	cgtataaacg	cgtaatatatac	tcgcgcgtaa	540
aacacgtata	cactatatac	acgcacgtata	cggaccgtat	agcgttatatac	gcgcgcgcat	600
attaatttac	acttatatac	gcgttaaacac	gatatatcac	acnccg		646

<210> 645

<211> 654

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(654)

<223> n = A,T,C or G

<400> 645

ncnctcggct	tggttttttt	tctgaccccc	ccccccccc	cccccggtcg	acaacgtgcc	60
caccgttgcc	atcccagcat	agctggttcg	ttctgtttta	ttcttagtag	tttagttcgc	120
ctatagtccc	tcgtctatcg	tctatcattt	aaggaggcgg	ggctcgtctt	ttagggcggg	180
tatcttaggt	attcttcttg	tttcggctgc	cgtctcggag	tctggtcctt	ttgctttcct	240
ttcttggtcg	aacttcgtgt	ttgatcgcgt	tgtttctttg	gggtcgtcat	acctaagggc	300
cacttcgcc	acaaacaagt	ttgtgtagtc	gtttctatta	gggttcgctg	gccggcgctc	360
tactgtgtg	gcgattttta	acgcgttttg	ttttaatttg	cttctccccc	tagggctcgc	420
tcggtcttct	ctctgttcgc	tgctctcgtc	cggccttttg	tgcggggata	gctccggcta	480
ttancgtgcc	gtgtccgtgt	ggnntttgtc	caatgtgaag	gcctaggggt	gcgggcttct	540
ttggccatgg	nttccctctt	tgtgancctt	aggggtaacg	antcgtaatt	naaggtcggg	600
ggttggnata	cgttntangg	gangcctgng	tccgntattc	cttgtttttg	cctn	654

<210> 646

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(645)

<223> n = A,T,C or G

<400> 646

tccttcggct	tggttttttt	tctgagcccc	ccccccccc	ccccacgcc	aagtacacag	60
accacacaaa	aacaacgtca	acacaacttc	gggtatacgg	accttaagag	agaccccgta	120
gtagacccta	ccacagccat	ccaatagtca	aacaacaagg	gcgcacccaa	tccatccata	180
gagctatcaa	acaacggagg	ggaaaggaaa	gagcagggtc	aacttagcag	agatcgaagt	240

230

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cggcactaat tcctttcaag tactcgctcg gctttagtgg cggggtaaaag tccgctctca 300
aagggccaac gaggttttaa agcgaccccc gtatcgagtc ttcttcgtat tcattaaggc 360
gttaaaggta cgagacctag aagagagtag aattagccca ccaaatcgcc taaaccggca 420
aaaacgacca aaagtcaaag acccttacia atatacactt aaaacgcaa ccccaaaaaac 480
gcgatcagta acgcacgtac ctttccacag cttttctttc tttcactctc caaaacaaac 540
ccgaatattt agcgcaaaaa atatccgagg gagaattaga agctattacc cgaaaaaaa 600
ncgganangg antaaatngt gggaatana cgtttggttt ttctg 645

```

<210> 647

<211> 753

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(753)

<223> n = A,T,C or G

<400> 647

```

accttacctg gtaccgggccc cccctcgag ttttttttt tccaaataca actcagattg 60
tatacgaaaa gctgataata cattgacttt tgctgtttaa atcccttgag ctttgataa 120
tgattttttt tgtgttaaca attgtagtat ataaaatcgg attcaccatc cttctgatgc 180
catattgatt agtttgattt tatggtgatg ggatcattgt gtgttaactg tattaagaag 240
aaatggattt gattgacttt gcatccattt ttatctgtgt tactttcatg ttttatttaa 300
aagcatttct ggaccagaat aagttaagtg gtataatttg ctttttacac gtttatataa 360
ttgaagttag caatgtggca aaatctctaa tggaaataaa atgcttcaga atgatgacat 420
aaatctgagc tatttcttgc ctggagaaca agtggtattc ataataattt aatagcttct 480
gaggtgtttt gttcatgtga tgaaggctta tccaccttgt atcaattcat gggctctgct 540
ttgtttaatg tagtcagggtt gttaatacna gacttaagag tcatcctact gtgataagtg 600
gtgagtgaag attacatgtc ttangaaaat tatactggga atatctctga cattaatggg 660
tttaaagtgt ttaaggctag gggatgatgc aatgganaan atncttccaa angtttctgg 720
ttgtttatat ttgnggaagn catnaagana ccg 753

```

<210> 648

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 648

```

gatatcccgg ggaatgcgg aggccttng gcttaactgt ttaccgcgta gggcaaagcc 60
ttgncaaatt cccggccagc ggagcggcga ggggtggggac tcacgggaag ttaaacagcc 120
tcgtcggcgt cctcgaggct ccaaaaccag gctctaggcg gggacgactg cagccgttat 180
ggaggccacc gcggtacgag ccgcggtgga ggcctcccca ggtggagcgg tggcctggag 240
gggaatcttg atcctgggccc agccacctgt caagaggagg cggagcgtca tgcctctgga 300
agactggatg aatattctcc aggagcctga cgaaggcgaa gaagtctttg cagaggaaat 360
tgaatgctgt ctgatgctac aat 383

```

<210> 649

<211> 349

<212> DNA

<213> Homo sapien

<220>

231

<221> misc_feature
 <222> (1)...(349)
 <223> n = A,T,C or G

<400> 649
 cgattgtnta cnagtcttag agtaagctta agntcgn tac cgagctcgga tccactagtc 60
 cagtgtggtg ggaattccat tgtgttggt cactagtata tggatttagc tagacanagg 120
 anatttaccc tattccattt agcacagtga gganaggcta nacagctagg atgcaataaa 180
 aaaaatttta atgagaaatg tgtgtggtag attaattcta ttaatctcaa gttatagatt 240
 aaaaaattta agtaccncat aaatgccatt tgcctttgct aangntacat ttttatgaan 300
 aangacntg catacnaat ganatactgg actttnggna cttgangga 349

<210> 650
 <211> 306
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(306)
 <223> n = A,T,C or G

<400> 650
 cattgtgttg ggagcatcct tccatcagct cccatgagaa attctctggt gggtttaagc 60
 aatccccaaa tatatcatat tgacatgaat atatcatctc ctcaatgtcc agcattagca 120
 gacaagatga gtgctgaaga tgatataact cctacctctt atgtaggcta gaggtaaagt 180
 ctggctctgc tgactgtggg gacataccga aaaggaaagt gggttaatat cagangacct 240
 ccctgcagat ccganantca ggnctggac tttctgggan aggaagcnaa aagttatntc 300
 tgaacc 306

<210> 651
 <211> 769
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(769)
 <223> n = A,T,C or G

<400> 651
 cattgtgttg ggcagggtca tttctaaggc atgggctgga agcttttatt taaaacttta 60
 catgtcttag aagcactctg gttgttgcta ggcagacaat ttacatctc ttgtataacc 120
 agttgcatga agttcatcat gcataattggc tgtggaaaac cttaacagca tcatgtcata 180
 aggtttcagt aaggtttaaa tgaaatcatg tattaagcac ttagtatagt gcaccttaaa 240
 tgttagcttc aaaacaatga caacctaaact aatgttgaaa gaagcttggtg tttgtaaatt 300
 atgtcttatt gaaagatgtc atcaaactcct gttatttcta atcccttaaa gtctctcaat 360
 gtattttctt ttgcatatc caatgacagg accttagttt aagccagtgg ttctctcaac 420
 ttctaatacca gagatacctg ggtgtcccca agaccttttc agagcatcct tgatgtcaaa 480
 accattttca taataatatt aaaatattat ttgctcattg tactcttatt ctctccaaa 540
 tattcagcga gttttccaga agctatataa catgtggtaa catcttatca ctctgacgat 600
 taatagaata tngnttttg gattcttgng tttaaaattt tctcactttg gggttctaatt 660
 atggnnacga ttaatagata tggntccat gaccagang ctttaaagca ntcaataatt 720
 ttaagagac taagnactat ctttaaaaga tngngaactc catcttaatt 769

<210> 652
 <211> 267
 <212> DNA

232

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(267)

<223> n = A,T,C or G

<400> 652

nnangccctt	taaccattgn	ggcctccacg	cnntggcggc	cgctctacaa	ctagnggatc	60
cgcnactcta	gnanaangat	tggctcttnt	gggntggggc	ggncgggctg	gggcgttaag	120
cggggctggg	cgcgcgccgn	ggttgnacna	ggcgccggcg	cccncacacn	cccggagcac	180
cctcnttgc	gccntncccc	gtcaccgccg	cgcgcgccgn	tccgcttttt	ccncacccan	240
agcncntttt	atctntgtct	cctccgg				267

<210> 653

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 653

cccnttnacc	cattgctgga	ctccaccgcg	gtggcgggcg	ctctanaact	agtgggatcc	60
ttncnatgag	atgngcgang	gaggacnnat	ttgctatnct	ggatggggct	gantcntnta	120
gctnctctag	cancagatgg	gttatcgagg	aagatgactc	caangggcta	nantcctatg	180
cnatccttaa	aanncancctg	ctgtnttcag	agtacgcgac	acatcatcnc	tnatgcattg	240
ntgancaaga	cgggcangtg	cttatcctca	gcgangatgc	ccttaaccan	gagctcgaat	300
ggacntatca	ccntanaggt	acannntnccg	caccacacac	cngcttgcn	cctgacgctg	360
gactggatcn	cttaggccac	caatnccccg	tttnccacat	ncctgggacn	ctananatac	420
tcganggggg	gccccgtanc	caattcgccc	taatactgag	ccttgntacg	nacgctnact	480
ngngtctcta	ttanaacgtt	g				501

<210> 654

<211> 710

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(710)

<223> n = A,T,C or G

<400> 654

gcgnctttan	cncatgctgg	gtccacgcg	gtggcgggcg	ctctacacta	gtggatccca	60
acactgagtc	caccacagna	aaactcanca	ccaggcagac	cccacaactg	cagaatccag	120
gctgcaattc	acagactaat	cntctagacc	cacctcagta	ccagatggta	ccacacagct	180
caaggnttta	ggtttgcgtg	gtanactcaa	tctctatctt	tcaccactgc	cagcctgact	240
tcagagatcc	tgngctctgg	acagtccctca	gtggcaggca	actctcagga	gcctcaggnt	300
tttggcacat	cccagnacca	gccagctgcc	acaggccctg	accttntanc	aacactgccc	360
atgtattcca	gacttctanc	ataccacagt	gccatgctga	ttgcatctat	agangctcag	420
gtgcncctca	aanctgtgcc	tgctgcagna	ngccccacgt	ctctggcatg	ccccaatgcc	480
atgngtggn	acanttgact	tctgggcatg	ntggaattcc	ctaccactga	ncctgaccat	540
aggnnggganc	ccattttttt	cgaggggggg	gccccggccc	caattccncc	ntatagnag	600
ncgtanttac	gcgcnnctta	ctnggccngt	ngtttaacaa	cgctcnntgan	ctgggggaaaa	660
cccctggngg	cnaccctaat	taaaacngcnt	tgcannacat	ccccctttcg		710

233

<210> 655
 <211> 202
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(202)
 <223> n = A,T,C or G

<400> 655							
ccccttttnc	ctttcanccc	ccccgttttg	gcngccgccc	acacctactn	catccaccca		60
cantcgacca	cccgagcttt	tttccgatcc	cancatcnat	gcngattttt	tctntgcntg		120
ctgngcctgc	acctttgnta	ggtcaagcct	ggcccatctt	cgacaacttc	ctcatcacca		180
acgatgaggc	atactctgac	ga					202

<210> 656
 <211> 308
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(308)
 <223> n = A,T,C or G

<400> 656							
gctgntgaaa	gaccacaccg	aaaaactctn	ctttccgact	tccacatgat	gatcngcatg		60
tgggtggtgag	agacttatca	tgacgacatc	gcttccnacc	atcgcanccn	ctgcccgaagc		120
ccattcatgg	aggcctgggn	antttctgtga	ntgacntnga	cnctanacnc	tnccactgtn		180
tgctatccag	acttgnttng	aatatnttat	tggcnaaana	canttncgga	atgctgtgnt		240
tgnncattga	angatctgat	cactatgaga	gggtgaggac	nncctgctng	ctggcantnt		300
ntaaccn							308

<210> 657
 <211> 696
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(696)
 <223> n = A,T,C or G

<400> 657							
accntttcca	caatnctggn	ctccccgcgg	tggcgccgcg	gtcgaccagc	aacctcagct		60
gtgggtcttg	ttacagtaat	gagttactgt	aaggaaagtg	tgacatttcg	agcaatttga		120
tttgtttaaa	aactagagca	gtttcagggt	tttccttgta	aatctgtctt	atgtgtcttc		180
aatgttcttt	cttgaggagt	agagaaagga	attgttagga	atgatgcata	aacctagggt		240
tattttatct	cgctgccacc	cataatcaga	gcagattctt	gggactatga	ccctcatgga		300
gacatgacaa	ttgtgtgtgt	ggtgggtggg	agaaaagagc	tgggaatttt	tagggtctag		360
agggtccaat	caggactatt	ttatggagct	ctgctcacca	actttaagtg	agcaccaggg		420
gtgngaaagc	gaatcttggg	ntcaaaaana	caatggnaag	gggtaagtgt	gtatnctgaa		480
ctggccactt	cggactctta	tttaactggg	tattctcant	taaggaggcn	nggggtgtct		540
tggtctgtna	aggaaaagcct	gtgcaatgga	atgactttta	aaccccccat	taaaaaaaaa		600
angntataaa	tcttgggtct	taanaangaa	gcctgggttc	tnttanccca	tttttcccc		660
gggaaggnaa	atnttcttag	gnaanggaag	ggaagg				696

234

<210> 658
 <211> 698
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(698)
 <223> n = A,T,C or G

<400> 658
 ctggactccc cgcggtggcg gccgctctag aactagtgga tccgtgttgg ctcaattctc 60
 aaggctgttg ctgtgcggcc tgttccccac acgtgctgct cagctcaggc aagcaccgag 120
 ctigtgttgt ttcattgctca gcgtggaggc ccctcctcca ggtcgctgct ctgtgggggt 180
 cccatacact caggctccta ggaggagtcc atttagaaag ccagggtttt tctcagagtc 240
 ttagttcctt gtgtgtcat ccatttcaca cgacttgggc cctgctcggg gcaacacagc 300
 aagagaaaaa acagggaaaa taagagaggg accttgaca cacacgctct ggaccacaga 360
 gccctgtgcc cagctcctct gtcaatacag gtggaatctc gtgcaggatc gcagggggtct 420
 gtgatgccac caaagagcag gccgggacag ggtaggaga gaaaggagag ggaagtgggg 480
 gtttctccta cgcactctta ttgagagag gaaaggcggg ttgtattgg ggtgtcgggt 540
 ctttgacccc acngcacagt tgtgagacac ccccatcctn agatcaaagc cccacataca 600
 gcttggggaa aaacaaaacn aaacaaaaca aaaacagtaa acctccatgc canttgttg 660
 gnaagttttn aatttncctc ccnaccan cttgcttc 698

<210> 659
 <211> 750
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(750)
 <223> n = A,T,C or G

<400> 659
 ncaantggn ctccaccgcg gtggcgcccg ctctagacta gtggatcctc ctcatgggcc 60
 tggatatctc tgaacatatg atgaacattg cttatgaaaa attatttgta ngaaaattgt 120
 gaggcctaag aatgntatct tcttttagtg atggtctttg ttgtctctg taaggnaactt 180
 gtgggcactc gtaagcttgg atctctttaa tctaatacca gntttgagat tttcttgcc 240
 ccatagatga attaaaactg gcgtacttct tgtttacaag anggataagt ctctagggt 300
 aagtcttttg ggggtcccaag tcaaaaagat gagggattta ccagttctct aaccttggt 360
 gccccagact ccaaactttg ccttctagtc ccaaggaggc atcaaaaagc aaaggccatc 420
 ttccaccttc ttttccanaa cagcacacat tccagacagt acttgaaagc aggaacctcc 480
 ttatccctta aaaacctctt ggaancatct tccctctctt gcttctacta tgcttggccc 540
 acctancatt cncntttttc tggaaaccgg aaaaancttn tgacttnngt tggctacatt 600
 cagcttggcc ccctacaatn tgggttccat ctgccctaan gaaattttaa agggcacttt 660
 tttnttggcc cctgactttc nnttttagg gctttcccc angctttgcc ctttgggta 720
 aagggttat tttccttccc ctttgggaag 750

<210> 660
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 660

tcggatccac	tagtccagtg	tggtggaatt	cgcgggccgc	gtcgacgggc	agtagtggtg	60
tgcntntcta	aatgttataa	ttatttcaga	attactctgc	cagaaagtta	tgatcataca	120
tagaagagtt	tgtagctaac	tttgaaagta	gtggaaagtg	gttttcatgt	attgtttggg	180
ttaattttaat	tttgattata	tttggttttt	agttcaggta	atTTTTTgt	tgaaaacttc	240
aaatgacaat	ttcttcatgg	ttactaaaga	tcactcatgt	ggagtagttt	cagatTTTT	300
tctgaataca	tgtattactt	ttagagatgt	aaagatgtga	aattactaag	agagaaaccc	360
atgtgatttg	tttagtggtg	caaaagtcgg	tagctccttt	gacctaagt	gccactgata	420
gttaaataga	tactgaagct	atgggcaggc	tggattgata	agaaaaagg	agacagagaa	480
atgggaaatt	gggaaagaac	tgtgcaaata	ggaaaaggag	agagcaacag	aacagaatta	540
gtaccacagt	gccgaagtgc	cacctcaggt	acttccatct	cccatctcct	gaagaattca	600
gtaacagttt	gcaaatggtc	aacacaatca	tttagtgatc	ctgggtgata	ttttcaatac	660
tttctgggga	tttcttggtc	ggnttcaaaa	gatgatgctg	atagttttat	tgccctgaa	720
ggtattctga	agnttancat	aattttattg	tcagtaaaat	atTTGaataa	aagngganga	780
agggaaatct	ggcntcttat	tttgggatnt	cngcnggggg	aangaggata	taattnacc	840
cggccttgg						849

<210> 661

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 661

aacttaagct	tggtaccgag	ctcggatccc	tagtccagtg	tggtggaatt	cgcggccgcg	60
tcgacctcca	ttcgtttctt	gtcctttttt	ttcatttttt	ctcatgttct	attcacttta	120
ggtttctaag	ataaatatta	taaaataatt	tttacttata	aattattcac	tgataccctg	180
tctttaacat	gtgaaatgaa	ttcaaaaagga	atcctaata	gaaataatat	actcatgatg	240
tttaatagat	ttgatttcga	aataataagc	cctctgaagt	cctaagttaa	aaataaagca	300
acttgtttga	taatttttca	tcaagaatgt	atctgagtct	ctgagtaatt	attagtagga	360
atattccatt	atcacaatta	cacagtataa	gctatttagt	ctaactttac	caaaaaagg	420
agctacttca	acactgtgtg	agacttttaa	tgggtttgca	ttgggtatgc	actattagca	480
agataaccta	ttttacagca	gtgttnttta	acctttccca	tttatttgaa	aggcagctaa	540
gatatagtag	ttaatntaan	gggctgatgc	atttatatta	catgtagana	atgggagata	600
cnaaaggagg	nggggggana	tnntttgnat	tcnnaagctt	cnntgncaat	taa	653

<210> 662

<211> 646

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 662

aaacttaagc	ttgtacccg	agctcggatc	cctagtccag	tgtggtggaa	ttcgcgcccg	60
cgtcgaccca	gggacaggca	gccagnctg	gggtcaccag	ggccccctct	tgggccctcc	120
aanagcaaca	gtactggcaa	cagctgggat	ttgctgagca	cagactctgc	agcaggctcg	180
gttgagctct	ctgtgcctgt	tccttcatac	catcctcacg	cccatccatg	agatgggtcc	240
agctgttttc	agatgagaaa	atggcacagg	aagctggtaa	gtgacagtca	gaaatgaatg	300

236

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ctggcagctt antccttga cccaccgcag tgcaggacct tgctcaacag ggatcacccct 360
tgtccgccac ctgttcatga ggccaccacag ggtttgtgtg gtcatttgtc tcctttcatc 420
tgcttgcctt caaccagctg ggtcattagg gctggggaac ccagacccca cacagtcctt 480
ctcccagang ccagacacan nctncgccac agnaaggact tcagtcctcg aancaaatgt 540
ncctgggcgt anaaactgna gggnccccaa tccctgggtg ggtactgctt tgcactggng 600
gaattcaccc ctcatgtnna acctttccct nttnncaccc ctaaac 646

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<210> 663
<211> 650
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(650)
<223> n = A,T,C or G

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<400> 663
aacttaagct tggtagccga gctcggatcc ctagtccagt gtggtggaat tcgcgccgcg 60
gtcgacgtcg acgcggcgng ccgtttcgac gcagttgata catattatta tatactacat 120
nggttttcta gaattaaaaa attaatgtgt agtgccagcc ctatagtgtaa gttacatata 180
tcaactctat ccaattttgt cagccataaa acttaccttt ttcacatact tctaactcta 240
acaatgtgag aaatgtagat cattgcaatt ataccacaaa ggcagatggc tacatgcaga 300
atggatagca gaatctagct acttacgcta gccacatggt agacgttttt tcctttgttt 360
ttgcaaaatt gcaatataag ttgcatatcg ttagagttaa aagatgtaaa gaacccatag 420
aagccagtgat tgaaggacat ttatattttc acctttacaa angaccttaa aattgcctat 480
gtggagcaga aactggagga gggcnaancc atcngtaaaa aaaattttgn tncattttgg 540
atttgggcac cattattacc tcccaggtt cctttttgnt ttaacctttc ttttaaaaaa 600
aataattcnt aatttttggg caaaaaaaaa caaggttttt attfaaattt 650

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<210> 664
<211> 678
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

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<400> 664
taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttta aaatgttagt ttgtcttccg ccatttctac 120
agaaagctgc aatttcaggt tttcaacctt ataggtgata tttaagaaaa aaaaaaagca 180
atcgcaaata gccccactgc ttttacaatt cttttttctt ctcttaggta tagcctgtca 240
ggtggcctaa tgtaattttt gacatctcta ggaattttta tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa 360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt 420
anaattatth taggactctg tggttttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggtcctga atagcccaa gcaacactga acaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat 660
cctatatthta cngcccnc 678

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<210> 665
<211> 694
<212> DNA
<213> Homo sapien

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237

<220>
 <221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 665
 ctttttcaa cttttttnct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60
 gacatctcta ngaattttta tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120
 ctttaagtgg gatttatgta tttctcaagc aagtgattaa agcaaaacta ggcacgattg 180
 aaatcaagat cttttaggca anaaagtcac gatgagtttt agaattattt taggactctg 240
 tggctttctc ttcataaaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat 300
 agccaaagca acactganca aaaagaacan agcaggggaag caacacacta ccngaattca 360
 aattatacta ccaggtgtga gtaacaaaaa cagcattcta ttggcataaa atagacacca 420
 agaccaatgg ancagaataa agaaccaccac aaataaatcc atatatntac cgccanctga 480
 ttatcaataa cnaacaccaa gaacatatnt taagggaant nctattcaat aantagtgtc 540
 ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agaccctat ccctcaccat 600
 acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660
 atnaaancta ctattaagaa aacagatcnc nccc 694

<210> 666
 <211> 705
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(705)
 <223> n = A,T,C or G

<400> 666
 tttaaaaatt tagatacact angaaaatta ttttagtata agaagaatat caggggggtgt 60
 agtactcacc agagctaaat gagagcgctt taaaaatgtt agtttgtctt ccgccatttc 120
 tacagaaaagc tgcaatttca ggttttcaac ctaatagggtg atattttaaga aaaaaaaaaa 180
 gcaatcgcaa atagcccccac tgctttttaca aatcattttt tctcttctag gtatagcctg 240
 tcaggtggcc taatgtaatt ttgacatct ctaggaaatt taatagaacc agaaatgggt 300
 gccagagata tgcctgcact aatcttaagt ggggatttat gtatttctca agcaagtgat 360
 taaagcaaaa ctaggcacga ttgaaatcaa gatcttttag gcaagaaagt catgatgagt 420
 tttanaatta ttttaggact ctgtggcttt ctcttcatag aaatagaaaa aaaaattgta 480
 taaaaccaca aaaggctcctg aatagcccaa gcaacactga acaaaaagaa caaagcagga 540
 agcaacacac taccagaatt caaattatac taccaagggtg tagtaaccaa aacagcattc 600
 tattgggcnt aaaatagacc haagaccaat ggaacagaat aaagaacca aaataaatcc 660
 atatttttac agccagctna ttatcaataa aaacnccaag aacnt 705

<210> 667
 <211> 817
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(817)
 <223> n = A,T,C or G

<400> 667
 nnangacttt tgtggtnnta tacaattntt ttttctattt ctatgaagag aaagccacag 60
 agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120
 tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt 180

238

agtgcaggca	tatctctggc	acccatttct	ggttctatta	aaattcctag	agatgtcaaa	240
aattacatta	ggccacctga	caggctatac	ctagaagaga	aaaaatgatt	tgtaaaagca	300
gtggggctat	ttgcgattgc	tttttttttt	tcttaaatat	cacctattag	gttgaaaacc	360
tgaaattgca	gctttctgta	gaaatggcgg	aagacaaact	aacattttta	aagcgctctc	420
athtagctct	gatgagtact	acacccctga	tattcttctg	atactaaaat	aatttttcta	480
gtgtagtcta	aactttttta	aaaagacatg	taatccgcgg	agtttgtaac	tcaaaacgag	540
tgcatctagg	aggtatcgca	agccgtttct	ggattaaatt	cccagctagc	ttgcttgctt	600
agcagggcgg	ggnaaanaag	acatctgcag	cctagggaag	aaaacctttc	gcattgttct	660
tacgtgttta	cgttatttta	tttctanaa	caaggcngaa	ttgggactcg	aatgggtcag	720
ttgggggtgg	ggatcccctg	gtncataaaa	ngtcanaaag	anggtacagg	cggaacncca	780
agggtcgtcc	tgcatttana	ctcgggaattt	tggtgcc			817

<210> 668

<211> 826

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(826)

<223> n = A,T,C or G

<400> 668

cggggggnnt	tacgtctctc	tggaagcgttt	tattgtacca	gggcgatccc	agcccaactg	60
taccattcga	gtccctactc	ctgccttgc	ctagggaat	aaaataacgt	aaacacgtaa	120
gaacaatgcg	aaagcgtttt	cttccttagg	ctgcagattg	tcttcttcac	cgccctgct	180
tagctagcta	gctagctggg	aatttaatcc	agaaacggct	tgcgatacct	cctagatgca	240
ctcgttttga	gttacaaact	ccgcggatta	catgtctttt	taaaaaagtt	tagactacac	300
tagggaaaaat	tatttttagta	tcagaagaat	atcagggggg	gtagtactca	tcagagctna	360
atgagagcgc	tttaaaaatg	ttagtttgct	ttccgccatt	tctacagaaa	gctgcaattt	420
caggttttca	ncctaataag	tgatatntaa	gaaaaaaaaa	acaatcgcan	atagccact	480
gcttttacaa	atcatttttc	tcttctaggt	atagcctgtc	aggtggccta	atgtattttt	540
gacatctcta	ggaattttta	tagaccagaa	atgggtgcc	gagatatgcc	tgactaatc	600
ttaagtgggg	atttatgtat	ttctcaanca	agtgattaaa	gcaaaactag	gcacgaatga	660
aatcaagatc	tttaggccag	aaatcatgaa	nanttttana	attattttan	gaatctgtgg	720
cttctcttct	taaaatngaa	aaaaaaattg	tttaaacc	naaggtctga	ataccaagc	780
nccctgaacn	anagaacaan	gccggagcac	cccctcccaa	atcccc		826

<210> 669

<211> 547

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(547)

<223> n = A,T,C or G

<400> 669

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aaactgaaat	tgacgctttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatttag	ctctgatgag	tactacaccc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagtttag	taactcaaaa	cgagtgcac	tnggaagtat	cgacgccgtt	300
nctggatnaa	attcccagct	tgctngcttg	ctnagccggg	gggcggtnaa	aaaaacatct	360
gcagcccnng	ggnaaaaacc	ttcgcatgtg	tcttacgtgt	ttacgttatt	ttatttcctt	420
nnagcaaggg	nggganttgg	ggactcgaaa	tggtacagtt	gggctgggga	tcgcccttgt	480
tacataaaag	ncgtccagaa	gagggacggg	tacaggcnng	ganctccaaa	ggtcagtcct	540

239

tgccatt

547

<210> 670

<211> 232

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(232)

<223> n = A,T,C or G

<400> 670

cgaactat	ttt agactaccta	ggaaaattat	tttagtatca	gaagaatata	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatgttag	tttgccttcc	gccattttcta	120
cagaaagctg	caatttcagg	ttttcaacct	aataggatgat	atttaanaaa	aaaaaaaagc	180
aatcgcaaat	agccccactg	cttttacaaa	tcattttttc	cccaacacaa	tg	232

<210> 671

<211> 214

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(214)

<223> n = A,T,C or G

<400> 671

ctcccccttc	ntccttcgct	actnncnatt	ttcnnaaatt	tntttcgcnt	atgnggaaaa	60
acacccacat	tnttcancct	gcacagaaca	ngnnnggggtg	tgtaaaatga	agggcttccn	120
cnctttctct	tattnaanaa	cactnaaana	gggangggct	aaaaccgcg	ngatntctac	180
ncatcgcgg	gcgcttttg	ngttggctag	aaga			214

<210> 672

<211> 328

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 672

ngancagcgg	ngtttaaacy	ggcctctaga	ctcgaggaga	cnctgtttgg	atggtggatc	60
acanntcgnt	actactatac	aggacagagt	atcggganct	cttggnrtgtt	ggngcctgcc	120
aaccactgct	nctgttaact	gcgtatctga	agggactcgg	actggcttca	gaagaactac	180
cggtctgaat	gnaccatgga	tgattcncnc	tagttgaaaa	aaaactcagg	cacatgtatt	240
gccactgatg	actagcgcca	gactnctctc	ggctctntaa	cgagcccaca	tgncngtgtg	300
ncncccgtag	tgntccaga	agaggttc				328

<210> 673

<211> 223

<212> DNA

<213> Homo sapien

<220>

240

<221> misc_feature
 <222> (1)...(223)
 <223> n = A,T,C or G

<400> 673							
gggggcaaag	ctggctagcg	tttaaactta	agcttggtac	cgagctcgga	tcccnagac		60
attgtgcatg	aaaatgcaaa	ttgagtgtgg	tctatantgc	catcntcacc	tnctgncngc		120
tcaaaacaac	ngctttctgc	tgcaatgggt	agggctcctn	acncacggtc	gcnnacggag		180
gccnncttat	cctcntcggt	nnggatccct	ngaagcatnt	tct			223

<210> 674
 <211> 256
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(256)
 <223> n = A,T,C or G

<400> 674							
gnnggggtcnt	ngatgagcgc	gcgtaatacn	atcacntnctn	ggcgnngntgg	gtaccggggcc		60
ccccctcnaa	gcggccgccc	ttttttnttt	ttttttcatn	acatgataan	ntctttnttc		120
taaacagacc	acaccactan	agttcctttt	ctttngtacg	gaattgagtt	aaagtagagn		180
atacaatgca	gggcttcnnc	tctatttcac	attccaggnt	ggttcngnat	ggatcgggcc		240
tgcctctccg	atgggt						256

<210> 675
 <211> 439
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(439)
 <223> n = A,T,C or G

<400> 675							
nnactagtcc	agtgtggtgg	aattccattg	tggtgggctt	gtatggggtt	ttttgtctag		60
ttntttggga	aatgttngtg	ttactatntt	ttggatatna	tatatgatat	gtatggccct		120
tctatgggct	cctcanacng	aactcaacca	ttttccacaa	aaccnattcc	tcctttccct		180
tcatgactga	gtggtgttgg	tactatccng	gaaactggga	cattgtcctt	cacatctntc		240
ccttanctgc	ctngtccnat	tgatgtcttt	gagctntgan	atgtctttgt	taactntctc		300
ctncntctgt	actgccggca	naattaagca	ccatntgtca	caaaaagtat	tgcgttacct		360
tcacgnatct	gttngttnc	atncttgctg	cttctccngn	ggaaaatagg	ctnttctggc		420
aaccgaacng	aanaaatac						439

<210> 676
 <211> 587
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(587)
 <223> n = A,T,C or G

<400> 676

241

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ngngngcctn  attaagcgcg  cgtaatacna  ctcactntgg  ggccaattgg  gtaccgggnc      60
cccctcaagt  tnatntgccn  aacctctctt  ttggaataac  aaaagggtta  acacatatgt     120
cctcataggg  acgcgctttc  acacnttcct  gacngcttca  tanacntcat  tncatatttct    180
cctcagnaca  agtttnaggcn  gaaggtgagg  canacnttat  aatttccatt  tcacaaatnc     240
ggaaagttag  gctcaaaggg  nttaaaaaat  aacctgatac  aantcataga  gccggtntct     300
ggaanaagca  ggagcaaagt  ccaggcatcc  tgatccaagc  tnggtccact  gccttccact     360
ctggagaggc  ttcattctccg  acaaaggaag  ggacntgagt  ggctgganaa  tctcatggga     420
taaagacctc  agnatttcat  gctcctggaa  atcccatggg  ttgaacaaca  ggtntttggc     480
ccgtggttct  ntccctttgn  ccatctttta  accttggggg  aaatgatggc  ntctntnagc     540
nttttttttn  aaagagatng  aaattgaatg  attatngct  cattggg      587

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<210> 677

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(444)

<223> n = A,T,C or G

<400> 677

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gtggggcatn  attaagcgcg  cgtaatacga  ctcactatag  gggccaantg  ggtaccgggc      60
ccccctcgaa  gcggccgccc  tttttttttt  tttttactgt  ccaaactntc  tatngatnta     120
gttgaactgt  ncaacgattt  catgaaattc  tatacacana  gccttcaggt  ccagagagta     180
aaacaaattt  aaatttnttc  accanattgn  agcagncana  agcatccnat  natatccgac     240
tacaatgaat  natatgctna  nggtanctna  tttaccact  ntggggctct  tanggtctgt     300
cacaaactat  tttcgtaaac  atcnntttta  anttnggtga  atggacctaa  tnccagataa     360
ntctatttna  tntacccatg  catnccgtgt  gctnactttn  cgggctgtgt  tggcntactt     420
ttaggagaaa  attggtataa  atnn      444

```

<210> 678

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 678

```

actagtccag  tgtgtgtgaa  ttccattgtg  ttgggagcag  tttaaaaaaa  aaaaagacna      60
aatatacnac  tcttgatnaa  acataaagg  acagtgtgtc  atgaggaana  gaaaagggtac     120
ctnaggatgc  aaaantacct  accacatggg  aaccgttngt  ccacactcat  tccnnanaaa     180
accgagtcct  ctcanttnca  cagtgtagc  tttcagttgg  gaagtgcctg  ccattactcc     240
naagcctaga  accttcacgt  cctgaagggt  ctggaagggt  tttcagattg  ctttaaganac     300
gcngcccttc  catattcttc  tccactacc  nggggaacgg  aacaaatgga  gctgcgacng     360
ggaagegtcc  cttcccttcc  gaacgctttc  tttcaaacct  gcctgccttc  cnggcgaatg     420
gaccggaagg  ttttctngct  tcctttcanc  ccnaattact  tcctgngttg  aaaattggcc     480
tgttggtttg  caaatgcngg  aatttggtta  ctttctcat  gtctgtgtgt  gnnncnaaccg     540
gctcctttgt  tgcctccctt  tngaaagggt  ttcacagggc  cccgcccttt  ctcttntaan     600
ngtcctaate  cggncnggac  cactcgggga  aaattttttc  ttttcgaaaa  gccgccccnt     660
ccgtccggct      670

```

<210> 679

<211> 449

<212> DNA

242

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(449)

<223> n = A,T,C or G

<400> 679

actagtccag	tgtggtggaa	ttccattgtg	ttgggagtag	gtctactaca	ncctacttcc	60
cctatcatan	aaganccttan	caacnttcat	gatccccccc	tcntanncct	tttcctcanc	120
tgcntcctag	tcctgtttgt	cctnttccta	acantcntaa	ganagatnac	taatnctact	180
atctctnacc	tccggaanct	acaanacgtc	tggaactatt	cngaccccat	gcancncat	240
ntcccatcgt	cctcccagcc	cctncccttc	ctttacntta	ctnaacgaag	gtcgacgac	300
cctccentac	ctcccnnc	attgggnccc	aanggnactg	gacctcacga	ntacaccnac	360
tacggggnga	ctaagnctgn	aactccttac	atatntcccc	gttacccecn	gaacncagcg	420
aacngcnaca	ccttggaent	caagaanta				449

<210> 680

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 680

tttcngtgtg	gtggaattcg	cgcccgctc	gacgagaaga	nggaggagga	naaggagaag	60
gagaagaagg	agaanaagga	ggagaaggag	aagaaggaga	agaaatcatc	atcatcatca	120
tcactgtct	ngcaactatt	taagtttgc	antcccttga	aaacaggtag	ttttgtttca	180
atgtttggga	ccactnctga	cnatgannag	aanaccaata	aatgcttgat	naatgaaaaa	240
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ccacaaaacta	tgatcctagc	atnaattggg	gcactctcaac	acctcaactc	cctgtgcaag	360
aacagatttt	caatgtctac	tgatgatttt	aaatggatta	nttcctctct	ttacttctta	420
agggcatgaa	gntttatgaa	acaaaactat	ncagttccag	acgcttaacc	cacatagtgt	480
taatagtcac	cttcaacaca	cnactaaacc	cccaaaaaan	gntttttacg	gngtttcgac	540
agttttcttt	tctttttgac	ttgnttaaca	cccnngacaa	ctttgtntcn	tttcntgaa	600
tcacancctt	cnaanancca	atggtncggt	tttttctcnt	tcngggccct	tccttnttn	660
aaaaccanac						670

<210> 681

<211> 494

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(494)

<223> n = A,T,C or G

<400> 681

tcatgggtgc	cacagtctga	tgtgagcgca	ttaaatttaa	ggatctccgc	ccttctcctt	60
aaaactcagg	acttggcaat	gancctagga	agcgcccctc	ccctccccc	ccanaccaa	120
gcccgggacc	gctgcgnctc	cagctgcgcc	tagtgaacc	gccgaattcg	aattcacact	180
cgnggggccc	gcgaagggtg	gcgcgcccgc	gggagcgccg	ggcgnagccc	gagggactgc	240
aagccaanaa	nggaggcatg	ggtggcgggg	ggcgccgtct	gatccaggaa	ggagcgagg	300
cgccgatcac	acactcttna	gacgcctctg	ccgcgcctgg	ccagcgcgca	gnctgcagga	360

243

cgcgcgaggc	aggaactcgc	tggagtttgc	caagccccan	gnctctggaa	agtntgtagc	420
tccctttcgg	ancgnctctt	ctggcccttt	gggacgggtg	tgtcattggg	cgggggtctg	480
tataaggggg	ggac					494

<210> 682

<211> 263

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(263)

<223> n = A,T,C or G

<400> 682

tgatcattca	agcgntgngc	gnataacgat	tgctnagccc	aacctttcat	agggtcgttc	60
ctttgggaat	nggatgtcta	ttgaatggca	gggatagggg	cactcggcat	tcgcctctgg	120
tacagttttg	catatatatc	ctcatcgcca	gcgagcgtag	gggancgtta	agtttgggga	180
aatgccnccg	catgnccctn	ccggagctta	aacccccaac	aatncccat	ttnaaaaaag	240
ntttnttant	taaaaaaaaa	aac				263

<210> 683

<211> 255

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(255)

<223> n = A,T,C or G

<400> 683

cttgcccggc	atgcacagac	ntntttacgg	acacnctact	ccaagngagc	ctgnanctgt	60
ctacgggtcaa	nccttaaggt	tnngcantgc	cacanatggc	atagtcccca	gggcggtnan	120
tctggantgc	tctctgcact	tgaacntaaa	gcgcntttca	aganaggnc	aatngcctgc	180
ctcttgacaa	cnaacaancc	cacaccnacc	tangaccctn	tangcaagga	ctggattctg	240
naaatgcaat	acaca					255

<210> 684

<211> 922

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(922)

<223> n = A,T,C or G

<400> 684

accttcatt	tcatgtgctt	ctattttcct	acatctttta	catgactaag	ggattaatga	60
aatcacctct	tcataatcat	gaccataatt	tcataccaaca	agtactcaag	tttgggtgta	120
gcactttatt	aatgcttacg	aattctctct	ctctccctct	ttctcttttc	cttagtcctt	180
gcacaataag	gatttttgaa	tgtataatat	catcttaggt	aagctttcat	atggtttttg	240
catatgaagc	ttatgactgt	cataagccat	accaagcctg	tggagtatgg	catgattttc	300
attacataat	ccaatgaaaa	tagacttatt	ttaaatccct	aactttgtag	ttttaatttg	360
tatttcacta	tcttgaaatt	aacagctagt	acttatccat	cacagcagtc	tcctactgac	420
atgaagcaag	ttgttgaatg	cagtaganca	tgaatgaaag	cattttaatgt	tanacaaaaa	480
tgggtgatac	ccaagcattc	tgaattattt	gcatcaagga	atgggacatg	tacattagt	540

244

```

gcatcatttc taccaatatg tgacttgaat tgttttttta aaaaaaggan aatgantttc 600
tcaatttgct ttaaaaaatt ttnaaaaagt tcaatggcat gctgctttgt ctggacttaa 660
tttattaaca attnttaanc cttccttaag gacanaattt tgggtgttcag gatcnccttg 720
aagggtctta tttttnatat nattccaaac ccaaaagggtg gtttaaaatg ggnggggttcc 780
ccccncaaaa atttggaaccg gcttttttat atttaaaaaa nttnccnttt gngtttgaaa 840
nctnaatacc aattaagggg gaattttacc tnccagtggg aaaaaaaaaac nctngccntt 900
naaaaaattc ccnggagnca at 922

```

```

<210> 685
<211> 531
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(531)
<223> n = A,T,C or G

```

```

<400> 685
tgaggctctg taaaactggt cctctgctag gcataacttca tattctctat attaaactca 60
tctttaattg gcatggaaga ttcaattgtc caaatctcag atgaagatcc tatattggat 120
gcaattaagc ctggcagcgc cctcaaaaga cagtcttgct actgctagcc acagccagga 180
cacagtaaca gttccttcta gtgacccnag accataanaa atananatct aaagaattct 240
gactccaaag gcattagccc attcctggta ttgccaatta tgatagaaaa aattgccaaag 300
ctcctgggac atggaaatac actcagtaca tttgagaact ggagaactan tttccaaaat 360
agtatgaaga catganggtg attgtagata tntgagtttg gagaanttga gggaaatcng 420
attacacatg ttactacaa gagatgttna taagtaaaga aggcctgata tacaatctaa 480
cagacnantg agataaatct taantcaca ctgacntccc ttttggggcg g 531

```

```

<210> 686
<211> 336
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(336)
<223> n = A,T,C or G

```

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<400> 686
ggngncctna tgagcgcgcg taatacgatc atatagggcg aattgggtac cgggcccccc 60
tcaagaacac tacaagctat gtctcttct canagagccc tgaantttta acatattgaa 120
agctctnatc ttgccaanaa actccactta acttcaaaac acaccctcca cacacatcat 180
gatcaactna gatcttactg aaccagaatc ctnaatggca tacttcagga acaggggtcc 240
anagaagcag ttctcaaant gcagctnaaa aagaaactga aaaccaatt catgcaanac 300
ctagggctta tttgagagca tttccagtg cagatt 336

```

```

<210> 687
<211> 271
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(271)
<223> n = A,T,C or G

```

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<400> 687

```

245

aatctgcact	ggaaaaatgct	ctaaaaataag	ccctaggtct	tgcatgaatt	gggttttcag	60
tttcttttta	agctgcactt	tgagaactgc	ttctctggac	ccctgttcct	gaagtatgcc	120
atntagatt	ctggttcagt	aagatctcag	ttaatcatga	tgtgtgtgga	gggtgtgttt	180
tgaagttnag	tggagtctct	tggcaagatc	agagctttca	atatgttnaa	acttcagggc	240
tctctgagaa	gaggacatag	cttgtagtgt	t			271

<210> 688

<211> 740

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(740)

<223> n = A,T,C or G

<400> 688

tgatgaagcg	cgcgtnntac	nactcactat	nggggcgaan	tatgggtacc	gggnccccct	60
cgaagcggcc	gccctttttt	tnnttttttg	tgagagttaa	aataaaatat	ttgagtttaa	120
tttaaagttt	gagtttaatt	aaaatataatg	gcatacccca	agttgggctt	tgcanaaaga	180
acacttctca	ggaactgtta	gttgggtgtac	caggaaactca	gaagggtcct	gttatttaaat	240
atatttgga	aatgcatgga	ttctctgaan	atcncctctgc	atgtgagcaa	cacttacatc	300
ncaaaccaaa	attggcattg	catacatnaa	ccaatatttc	ccaacattt	ctggttatgg	360
cccacccct	ttgtgtanta	cttattgctg	ttttttggaa	ccctggggaa	attacttaaa	420
atattcagct	ggaaattaca	ggcgttactt	ttaaggganc	aagaattaca	gtgactccca	480
aaattgcaag	tggtgattac	tatttaagaa	ccaagaatt	tgaaagaaat	tttgaaaagt	540
gaaaacngga	aatnttaaat	gacttctcaa	atittgaaaa	ctcnggnaaa	catctccact	600
ttggtncct	tccttttaaaa	attggctaaa	aattntttnt	tatncccacc	ccattggaan	660
tnccccccc	ctggaacaat	tggattcccc	tatttcctaa	aaaacggccn	ccccccccg	720
ggngaacncc	nacnttttgn					740

<210> 689

<211> 635

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(635)

<223> n = A,T,C or G

<400> 689

actagtccag	tgtggtggaa	ttccattgtg	ttgggattac	atatactttt	agcaattttt	60
aaagaagtgt	acaaagttga	gatgtttcct	gagctctcat	atatctgana	atgtcatttt	120
acatctccgt	cttcacctct	caaaacttct	ttcaattctt	tggtctttaa	tagtaatcaa	180
cacttgcaact	ctggagtcac	tgtaattctt	gctcctttac	agctacncct	gttattttcca	240
gctgaatatt	tttagttatt	tcccaggggt	ccaaaaaaca	gcaataagta	ctacacaaag	300
ggggtgggcc	ataaccagaa	atgtttggga	aatactggct	catgtatgca	atgccaaatc	360
tggtttgcna	ttgtantgtt	gctcacatgc	agagtgaatc	ttcaanaaat	ccatgcattt	420
tcacaaatata	tttaataaca	gggaaccttc	tganttcctg	gntacaccaa	ctaacagttc	480
ctgaaaaaatg	ttctttctgc	aaaacccaac	ttggggatat	gccatatatt	tttaattaaac	540
tcaaaacttta	aattaaactn	caattatttt	attttaaaact	cctcaaaaaa	aaaaaaaaaa	600
agggggggcc	cttccaangg	ggggnccggt	tcccc			635

<210> 690

<211> 3923

<212> DNA

<213> Homo sapien

<400> 690

acagaagaaa	tagcaagtgc	cgagaagctg	gcatcagaaa	aacagagggg	agatttgtgt	60
ggctgcagcc	gaggagagcc	aggaagatct	gcatgggtgg	aaggacctga	tgatacagag	120
gaattacaac	acataacttt	agtgtttcaa	tgaacaccaa	gataaataag	tgaagagcta	180
gtccgctgtg	agtctcctca	gtgacacagg	gctggatcac	catcgacggc	actttctgag	240
tactcagtgc	agcaaagaaa	gactacagac	atctcaatgg	caggggtgag	aaataagaaa	300
ggctgctgac	tttaccatct	gaggccacac	atctgctgaa	atggagataa	ttaacatcac	360
tagaaacagc	aagatgacaa	tataatgtct	aagtagtgac	atgtttttgc	acatttccag	420
cccctttaaa	tatccacaca	cacaggaagc	acaaaaggaa	gcacagagat	ccctggggaga	480
aatgcccgcc	cgccatcttg	ggtcatcgat	gagcctcgcc	ctgtgcctgg	tcccgtttgt	540
gagggaaagg	cattagaaaa	tgaattgatg	tgttccttaa	aggatgggca	ggaaaacaga	600
tccgtgtgtg	gatatttatt	tgaacgggat	tacaagattg	aaatgaagtc	acaaagtgag	660
cattaccaat	gagaggaaaa	cagacgagaa	aatcttgatg	gcttcacaag	acatgcaaca	720
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taagaactct	gagtgatatc	aacattaggg	attcaaagaa	atattagatt	taagctcaca	2700
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<210> 691

<211> 882

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(882)

<223> n = A,T,C or G

<400> 691

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aaaataaaac	tagtataaag	atagaagccc	agggttgatt	taagtctgcg	gaaatcataa	180
accataggtc	agactttctca	ttgatgaggt	acttggtggg	tagaatataa	ttaggtatat	240
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<210> 692

<211> 235

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(235)

<223> n = A,T,C or G

<400> 692

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cttctcanag	cacttaatat	gttaatatata	aactncngna	aaaaagatnt	tcnatgaanc	180
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<210> 693

<211> 383

<212> DNA

<213> Homo sapien

248

<220>
 <221> misc_feature
 <222> (1)...(383)
 <223> n = A,T,C or G

<400> 693
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 taatgcaccg catctacatt cccatgctct ctttacttct tcagcattgc cttaaaggcat 180
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 ctctgtccat aatggnaaac ctgnatgatc cttgatatta acantttaag gaatgctcat 300
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<210> 694
 <211> 204
 <212> DNA
 <213> Homo sapien

<400> 694
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 aagaaccctg tctgatgaag catcatttca gaattttaag tcaacttaca aatgtggtat 180
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<210> 695
 <211> 670
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 695
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 cagggccacc caaaaggagg aagccggaag gaaaaaacag gggccccca aaggaggaag 600
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 ggggcccnnc 670

<210> 696
 <211> 317
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(317)

249

<223> n = A,T,C or G

<400> 696

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gccactgtc	atcgtggata	catttcactt	ttttcacatg	actaaggagc	tctccggagt	180
gaagagttag	taaataatgtt	tattacgcat	tcatttgcta	agaatcatca	agaacccaaa	240
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<210> 697

<211> 246

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(246)

<223> n = A,T,C or G

<400> 697

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tttttttctc	tnacagagnt	ntttttgtgc	ccttggttct	tatgctcana	ctcngcaaaa	180
aanatcaaaa	gntacnnatg	aaaaacntat	nccatctnca	naaaggaggt	gnagntatta	240
ctttct						246

<210> 698

<211> 3674

<212> DNA

<213> Homo sapien

<400> 698

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agccagtga	acataattcct	tcttctctcc	atcaggccaa	atcacggtgt	tgacctggc	180
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250

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<210> 699

<211> 2051

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(2051)

<223> n = A,T,C or G

<400> 699

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<210> 700

<211> 2841

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(2841)

<223> n = A,T,C or G

<400> 700

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252

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<210> 701

<211> 3228

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(3228)

<223> n = A,T,C or G

<400> 701

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Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly
      50              55              60
Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu
      65              70              75              80
Tyr His Arg Glu Lys Gln Val Leu Ile Gly Gln Trp Val Glu Ser Gly
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260

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 35 40 45
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Glu Ser Leu His Pro Pro
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 Lys Lys Arg Ile Pro Arg Thr Tyr Pro Ser His Leu Trp Ile Pro Gly
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 145 150 155 160
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261

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262

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263

ctcactatnc ggcancgcag gcgcagcagg gaanggggtca cctcccagtc tc 112

<210> 715

<211> 326

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(326)

<223> n=A,T,C or G

<400> 715

tactctanag gatctncgng tcatntggat tctatntcga ctcactctag ggctcnagcn 60
gtcngccggg caagttattc ggatcgtcgg gntccgagct tcgcaattaa ntgtgccatc 120
gttctncaac gttcctgact nggaancccc ngcngttcng atccnnggt acctagctcc 180
anntccccg tntccttctt ggngtntcat naangaggac cncctcgcg cnccttctc 240
taatctgcnc acnctgaacg nccaatggac atngtgcgtt taatntanna ggcccgnctc 300
gngtgccctt cccgtnannt cagctc 326

<210> 716

<211> 122

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(122)

<223> n=A,T,C or G

<400> 716

nntgcgtcgc ctgngcgtnt actctagatg atctgantag tcatatggat tctaatacga 60
ctcannatag ggctctagcg nggatncnga ttcgtcntcc ngattcantg acnccggtan 120
ca 122

<210> 717

<211> 203

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(203)

<223> n=A,T,C or G

<400> 717

cntgcatgcc tgcaggtcga ctctagagga tctactagtc atatggatcg agcgcccgcc 60
cgggcaggty tnaatgataa anatgcatca tactanccta cagaanggag agataatgtt 120
ngntggacca ngttggtttt cttgcgtgtg tgtggcagta gtaagttatt agtttttana 180
atcantaccg ccctccgcac cac 203

<210> 718

<211> 168

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

264

<222> (1)...(168)
 <223> n=A,T,C or G

<400> 718
 ggcagganga tēncttgagc ccngagggtc gaggtacag tgagccanga gtgcactact 60
 gtinnccgctt ccgcatncac gngtggtccg atccccgggt accganctng anttactgg 120
 anttcttttt aancgtnttg antggtacna cctcagantc cctggctg 168

<210> 719
 <211> 210
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(210)
 <223> n=A,T,C or G

<400> 719
 cancgctcnc ataacacgta tttntgatn aagattctna ctgacccatn aantctacnt 60
 ctcaagctct tncanngtcc agtnaangga atgtgtatnn gtngggatnc cacanaaaaa 120
 aganatntcg gncgcttcat tantcatcct tcttaccan ntctctngat nncagtntg 180
 ancntgaacg cācāctacng gatntctcca 210

<210> 720
 <211> 131
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(131)
 <223> n=A,T,C or G

<400> 720
 tccatcctaa tacgactcac tatagggctg ccaacctgcc atccactact gaggaagacc 60
 cgnanactta ggggtcact gcgagccacc ggccacaggt cgtatagggc aaagcacng 120
 gaagcaccct t 131

<210> 721
 <211> 121
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(121)
 <223> n=A,T,C or G

<400> 721
 tccatcctaa tacgactcac tatagggccg ntgantnctg gcgaaaggct tacaattaag 60
 naggaaaaan ganccaacaa ctaaaaaaaa nncggncgtg ncagcttnga tgactngtcc 120
 a 121

<210> 722
 <211> 246
 <212> DNA
 <213> Homo sapiens

265

<220>

<221> misc_feature

<222> (1)...(246)

<223> n=A,T,C or G

<400> 722

```

aactggagtc gcgcgctgca gtcacattgt ggatccanaa aatcggcaca agctctcntg 60
gnttcntcga tatgaanaac actaatccca tgtngtntgn gtctccgtga ttcattccctc 120
gcacnggtcc cnttccnaac cnttgcatag gtgttatgtt gtantctccc cagtgcacaa 180
agattnacac tctctcantg tctganatat gcacgagttc attgtcctgt cncctgnaac 240
atcaag                                     246

```

<210> 723

<211> 160

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(160)

<223> n=A,T,C or G

<400> 723

```

cctccgaaa atccaantag agtaantncn ctctaattccg gggnaattgg nggggttnnat 60
acgtcctcct cccccagnt aggattnana aaaggntcc cagancaaaa nctccaaagt 120
gnatcnanta gccgtncctg anatncaacg ccctacgtc 160

```

<210> 724

<211> 156

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(156)

<223> n=A,T,C or G

<400> 724

```

tnanccnata tacaccaaatt tctgattcta aantcccacc caagggaaaa aagttgagaa 60
gagcctttcc acttttctac taataaaaaa atgcaccagc ccctaccann agtgnggaaa 120
acctccttag gcccttgnnt ggaacaancg aaaatc 156

```

<210> 725

<211> 347

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(347)

<223> n=A,T,C or G

<400> 725

```

aganggttnt atncatgctg tactcgcgcg cctgcagtcg aactagtgag atccaaagaa 60
ttcggcacga gagacggtgc gcgatggacc gagggcccca gccgngagg cgcgcgcgcc 120
gagcccgcg ncagacgccc catcagtagc gtccgcaccg ggnagccgag gntctcgccc 180
gagccgtggg cgcgcccag gagcgggctc gcctcccgcc gtccctcgca gctctgcgag 240

```

266

```

gcccgagccc gcgcgcgcgc cgcgcgcgc ttgccgcgcg gccgcgcgcg nccggnaaac 300
gcggtcgagg tctggatgng gcanngcccg cncctntcgc tgagcct 347

```

```

<210> 726
<211> 162
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(162)
<223> n=A,T,C or G

```

```

<400> 726
ttgggtgggt tgggtggggg naaatttncc catttgggtg ggtttggggg ggnaaatact 60
tcccgccctt tnggtnccca aaganacnaa gggggagtc cttnatagag gnagncgcat 120
ncntcncaac nactngact ttgnccatgg ggagnaaggt gg 162

```

```

<210> 727
<211> 120
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(120)
<223> n=A,T,C or G

```

```

<400> 727
tgttgggtgg ggaattccat tgtggttggg ggnaaatctc cgcttgtcca aagnacaggg 60
ggggtcnctt anagnnagg gggttcctcc ccaccacttg ncttgnccat tngagnaag 120

```

```

<210> 728
<211> 130
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(130)
<223> n=A,T,C or G

```

```

<400> 728
gaccactgc agcgttnaac ttagcttga ccgagctcgg atccctagtc cgtgtggtgg 60
aattccatgt gtcgagagag gggcaaatac nctccaanac ancncctca tgctcnacac 120
atattcgcat 130

```

```

<210> 729
<211> 182
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(182)
<223> n=A,T,C or G

```

```

<400> 729

```

267

```

cngactgctn gcgtttaaac ttaagcnagg taccgaacgg ggatnnacga ctantgatcg 60
gctggctgct tccagtcgat tanatttgtg aaaaagctga accncngccn gttaaggggg 120
annatgcaaa anatncatcc nnctgccccn taaactgntc tntccnaggg aaaaaangga 180
ag 182

```

```

<210> 730
<211> 678
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n=A,T,C or G

```

```

<400> 730
cactcncact ccggacctag gcnettcacc actgctctct tctctctcct cctcctcntc 60
ctcggggctg ggggaccttc ccagtgacc atctcacttt ggctgaancc cactcggggc 120
agcctgagtt tggggctctt ggccttctca ccctcctcgg cccctcctt ggcccgacc 180
aggccaaacc ggggcagccg taccttgagc ttgtgtccgg cctctccctc cccctctgcc 240
acctgggtact cggcatgggt gccccggga tggcgagagc tccacgtcgg gcagtggagaa 300
gcagaaagta cgctcggccc ctgggggctg ctctcagca cctcggccc ccacctagc 360
tctggccccc agtgtgggca acttcagcct cagcccacc tcgctgtgg ccgcctcggc 420
cgctgtgcc tctcggtta gcccacgtc caactcaagc tggggcactg tcacggtggg 480
catcttaaag acaccctcac ccaccagcag ctaccacct gcaacctggg ctccaggcaa 540
aaaaagggtc acctggggca nctgaaccct gtacctgctg tgccctctgc tgaanggaat 600
gttatctgaa cctgctgccc tgggggtact gccttcccaa aaccgggtca antccacctg 660
ttggaaggna aatncccc 678

```

```

<210> 731
<211> 135
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(135)
<223> n=A,T,C or G

```

```

<400> 731
gagatccgac gtcacccctc tccggcggcc caagacgctg caactcccga ggcngcccaa 60
atatctttgg aagagcgctc ccagcccaac acaatggaat tccaccacac tggntagtg 120
gatccgagct aagcc 135

```

```

<210> 732
<211> 660
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(660)
<223> n=A,T,C or G

```

```

<400> 732
gcttggtacc gagctnggat ccctagtaac ggccgccagt gtgctggaat tcggctttct 60
tcaatcagnt nacgagctgc atggtctgct aacattgtca taattgctgg catagattac 120
tgaaaataaa gaaaaaaaaa tgaagctgcc tatcaagttt tggattattc aaaaacttcc 180

```

268

```

tacaagttat tttacttcaa ccatgttatt acaaataatt taatgaatac tttagagact 240
ttaattacaa aaaactgaga tagtaaaagc aagtaataaa agctgaaatt acttagctat 300
ttgataatta cataaattat tatggtccat tcaacttttc tagtgtttag tttatacacc 360
aggaagactt tcctattcta ctaacattta taaagtatgc taacctatta tttaaacgca 420
tccactatta ggattttatg gcctaaaacg tgatacagtt cagtatcttg atgtcaaaac 480
tttttaagca agtagggatt aagttcaagt gaatgtgatt ttctttcttc ccagtagggg 540
cttctgaata actcagnaana gctcacttcc attatcttac tttataaaaa aatgctataa 600
gacagaatgg gccgacgtgg nggctccacc tgtatccacc tttggaggcg agnggcgaat 660

```

<210> 733

<211> 836

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(836)

<223> n=A,T,C or G

<400> 733

```

aattaatgac tttttttccg ccctgccaaag ctagtttgtc taaatataat gtaaagaaat 60
tagctactca ttttctggtc cacgaagggt cctaaaatgg gaagaagtgg agatctgacc 120
ttggttagttc taaatacact aaactgggag tgccatggat ggctttcagg atgtcctgaa 180
tcctctataa ttgtatacaa aatcgtgagt ttttaaaaac tggggttagag ctattgggttc 240
ctcagagtct caggcatctt agaccccaaa aaaggttaag gactactgac ttaaccaatt 300
aggtttgagt ggcattggct ttgaagaaaa gcagaggaaa gatataattt ataattcttg 360
gcaacaaaaa agtggatgtg tgccagcatc ttagagtaga atcctcttaa aaggatagca 420
ctgcatatga actagtaggt ttttaaccagt gcatatttag gcgaagtagc tcatttttct 480
gttagaattc ttttttattt gggaatgggc aagcttttac agcttttacc ttgccaatga 540
atacctggaa tttaaaaaat cttgttaggc atattgccca taaagttttt tttcctagat 600
catatattca gtaaatatgt ttgtagcttt atttcaatcc cccaattcat tgagggttga 660
aacaatttga atggtttgag tgtagaagct aagttatttc tgtagaggct aagggcattt 720
ataccaanat atgttagact tgnngntcct gtttaaccatg ctgtanacaa taggaattac 780
tgtatatcca cattttaatt ttaacatctt ctgctttgnt gntgggttga gangga 836

```

<210> 734

<211> 694

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(694)

<223> n=A,T,C or G

<400> 734

```

nagtntatt tncactaaac tgnagtgcc ttggatggct ttcaggatgt cctgaatcct 60
ctataattgt atacaaaatc gtgagttttt aaaaactggg ttagagctat tggttcctca 120
gagtctcagg catcttagac ccccaaaaag gttaaggact actgacttaa ccaattaggt 180
ttgagtggca ttggctttga agaaaagcag aggaagata tattttataa ttctgggcaa 240
caaaaaagtg gatgtgtgcc agcatcttag agtagaatcc tcttaaaaag atagcactgc 300
atatgaacta gtaggtttta accagtgcac atttaggcga agtagctcat ttttctgtta 360
gaattctttt ttatttggga atgggcaagc ttttacagct tttaccttgc caatgaatac 420
ctggaattta aaaaatcttg ttaggcataat tgcccataaa gtttttttct ctagatcata 480
tattcagtaa atatgtttgt agctttattt caatccccc attcattgag ggttgaaaca 540
atttgaatgg tttgagtgtg gaagctaagt tatttctgtg gaggctaagg gcatttatac 600
caagatatgt tagacttgtg gttcctgtta accattgctg tagacaatag gaattactgt 660
atatccacat ttttaattttt aacatcatte tgtc 694

```

269

<210> 735
<211> 126
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(126)
<223> n=A,T,C or G

<400> 735
nonttgaaac nggttgacca gacttcaggc ctgtgcgctc aatcgtggag aatctcgtgc 60
cgaattcggc acgagtctct ctctctctct ctctctctct ctctctctct ntctctctct 120
ctctct 126

<210> 736
<211> 165
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(165)
<223> n=A,T,C or G

<400> 736
cagaagcctt taaaccgggt ngaccagact tcaggcctgt gcgctcaatc gtggagaatc 60
tcgtgccgaa ttcggcacga gtctctctct ctctctctct ctctctctct ctctctctct 120
ctctctctct ctctctctct ctctctctct ctctctctct ctctc 165

<210> 737
<211> 125
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(125)
<223> n=A,T,C or G

<400> 737
ggnagcccct ttaaccgttt gtccagactt caggcctgtg cgctcaatcg tggagaatct 60
cgtgccgaat tcggcacgag tctctctctc tctctctctc tctctctctc tctctntctc 120
tctct 125

<210> 738
<211> 137
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(137)
<223> n=A,T,C or G

<400> 738

270

```

ggagnncnctt gancaggatg accgacttca ggcctgtgcg ctcaatcgtg gagaatctcg 60
tgccgaattc ggcacgagtc tctctctctc tctctctctc tctctctctc tctctctctc 120
tctctctctc tctctctc                                     137

```

<210> 739

<211> 970

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(970)

<223> n=A,T,C or G

<400> 739

```

aggcctatatt aggtgacact atagaacaag tttgtacaaa aaagcaggct ggtaccggtc 60
cggaattcgc ggccgcgtcg acggcccttn gtgccactag ntctttcatt cttccccccc 120
atcaatcagt gaacttttta gcctactcaa agctttgctc caatgcatag gatttatgat 180
tgtggggatt tccagataat ataaatattc aacatgaata ttttaaatta aggcattgaga 240
cattttttcct aactgagcat agccatgaac ctctcacgtc tgttcctctg tgtcagtttg 300
tancactgaa tacagcagcc ctctctaaaag tccaggcagt gcacaggctc tgacatgatg 360
aagtgcgtg ttgctatggt gattttgcag ctggccaaa agtcactggt tgattttacc 420
cagcaggaga tttttgcaaa aatttccttg gtgagagtga aatcaaactc ctattttgnt 480
tctcctctgc aagctgnagt taagatggat taatgagtac ttttagatta attaactctg 540
aagagaaaaat gggagaaaag tgaggaaggt tgttggcaga agtcattgct ggaatccttc 600
tgaagggagt actgacttca cttgcaaaga cnagagacta naagacaatg aagttaaact 660
tggcctgtct ctcatatgat agatgctgag agtcaggntc agggaaaattt aattctgtca 720
tacgcataatn ggattatgtg gtcattggatt tgttggcact aaccngcctn taatcagnat 780
aagaaaaagt ttttggtaga naaagaaaat tatggcccag aaaaacctgg aanacttgga 840
aaaaatgntn gggggccttg ggtggtggtc tnaaaanacc ccctggggat nttaaacc 900
aaantgaaga agggaaaaat ntttccccnt nttttntttt tttgccccct tgggattggn 960
ttttntttcc                                     970

```

<210> 740

<211> 739

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(739)

<223> n=A,T,C or G

<400> 740

```

gntgtcnaaa aagcaggctg gtaccggctc ggaattcgcg gccgcgtcga cggcccttgg 60
tgccactagt tctttcattc ttccccncca tcaatcagtg aacttttttag cctactcaaa 120
gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180
acatgaatat tttaaattaa ggcattgagac atttttccta actgagcata gccatgaacc 240
tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatgggt attttgcagc 360
tgcccaaata gtcactggtt gattttacct agcaggagat ttttgcaaaa atttcctggg 420
tgagagttaa atcaaaactcc tattttgttt ctctctgca agctgnagtt aanatggatt 480
aatgagtact ttttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
gttggcagaa gtcattgctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600
aagagactan aagacaatga agttaaactt ggcctgtctn tcatatgata gatgcttgag 660
agtacaggnt cagggaaatt ttaattctgn catacgcata ttggattatg tgggtcatgg 720
ctttgtttgg cncctaacc                                     739

```

271

<210> 741
 <211> 1171
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(1171)
 <223> n=A,T,C or G

<400> 741:
 gccttgnggt gacactatag aacatgtttg tacaaaaaag caggctggta ccggtccgga 60
 attcgcgggc gcgtcgacgg cccttnntgc cactagtctt ttcattcttc ccccccacatca 120
 atcagtgaac ttttttagcct actcaaagct ttgctccaat gcataggatt tatgattgtg 180
 gggatttcca gataatataa atattcaaca tgaatatatt aaattaaggc atgagacatt 240
 ttctctaact gagcatagcc atgaacctct cactgtctgt cctctgtgtc agttttagc 300
 actgaatata gcagccctcc taaaagtcca ggcatgtcac aggtccttgac atgatgaagt 360
 gacgtgttgc tatggtgatt ttgcagctgg ccaaatagtc actggttgat ttaccaccagc 420
 aggagatttt tgcaaaaatt tcctgggtga gagtgaatc aaactcctat tttgtttctc 480
 ctctgcaagc tgtagttaag aagggattaa tggagtactt ttaagaatt aaattaacct 540
 cttgaaagaa gaaaaaatgg gggaagaaaa aaagtggaag ggaaaagggn ttggttttgg 600
 gccnaaaaaa aagttccaan tttnggcntt ggggaaaaat tcccctttt ccttggnaaa 660
 aggggggnaa ggttaancct tgggaacctt ttccnncct tttnggcca aaagggggaa 720
 ccanggggaa agaaccttta ggnaaggaa acccatttgg gaanggggtt naaaacctnt 780
 ngggcccccg ggccctcctc caanaaggga aaaaaaagg cctggaaaan gtaccagggt 840
 ttcangggna aaanttaaaa ttcttgcca atancncat aattgggaat tatggggggg 900
 ccattgggctt ttggtttggg cnccttaacc cgcnttttaa attcaaanna aaaaaaagng 960
 gtttgaaaaa nnaaaanaaaa aaaattnaan ggnccnnaaa aaaaaccctg gaaaaccttt 1020
 ggaaaaaat tngnnggggg gccntttggt tgggggggtt tnaaaaaacc ccctnggggg 1080
 ttttttaagc ccaaaagggg gggaggggna aaanggtnc cttntttttt ttttnngccc 1140
 cccttgggga atggnttant tcangggggc c 1171

<210> 742
 <211> 739
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(739)
 <223> n=A,T,C or G

<400> 742
 gntgtcnaaa aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cggcccttgg 60
 tgccactagt tctttcattc ttccccncca tcaatcagtg aacttttttag cctactcaaa 120
 gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180
 acatgaatat tttaaattaa ggcattgagac atttttccta actgagcata gccatgaacc 240
 tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
 ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgcagc 360
 tggccaaaata gtcactgggt gattttacc agcaggagat ttttgcaaaa atttcctggg 420
 tgagagtga atcaaaactcc tattttgttt ctctctgca agctgnagtt aanatggatt 480
 aatgagtact tttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
 gttggcagaa gtcattgctg gaatccttct gaaggagta ctgaactcac ttgcaaagac 600
 aagagactan aagacaatga agttaaaact ggcctgtctn tcatatgata gatgcttgag 660
 agtacaggnt cagggaat ttaattctgn catacgcata ttggattatg tgggtcatgg 720
 ctttgtttgg cncctaacc 739

272

<210> 743
 <211> 610
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(610)
 <223> n=A,T,C or G

<400> 743
 ctgtccttat ttcttttagca aaaatttccc aagagaagaa ttgctgggat aatgcacatt 60
 taaatttttg atagacattc ccaaataatta tacctgtttt tgagaccttt aattcctgtt 120
 gtcaaattgc cctatatatg gagtaataaa cacgatttaa agaaatgagg actaaaaaaa 180
 gatttatatat aacccaacat aaaggcaacc tcttaggcgt tgacagaaac tgacaacttt 240
 ttatctgtgg gtgcgatcca ttataagtaa cctgagcacc ttatTTTTTc tttttaaaact 300
 ctaggtagga taccgagggt ccacaaattt ttcataagaa atatTTTTTc tctgccctat 360
 gagatttttaa aaaatattat actgcttcaa ttgcatcaaa agaaatggac cctaataatct 420
 atgatgaagg atttggagtt agaagacctg agtttcaatt ttggcatggc tgtttgtcta 480
 gctctngat cttggacagg tcaattgact tggcttaatc ttctcatcca tttagnggag 540
 acagcaccac tattcacagg actattgncn gaattaccag acaatagcat agngaaaaat 600
 ataangcctt 610

<210> 744
 <211> 127
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(127)
 <223> n=A,T,C or G

<400> 744
 ttnacctccc tggaccgggc ccccttccc cgggcggnct ccccgggctg caggaattct 60
 gcacgaggga gagagagttn gagagagaga gagagagaga gagagagaga gagananaga 120
 gagagag 127

<210> 745
 <211> 458
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(458)
 <223> n=A,T,C or G

<400> 745
 gatatcccgg gattcgcggc cgcgtcgacg tggcctctag tttgtcctgg tccaaagcag 60
 ggaagctggg ctacgtcctg ccaggtcag ccttaggtta agggctgcct gggggaggga 120
 acttctctgg ccttcgggtc tctgtgcaact ggggtggctc ctgtggccca gaatgccctg 180
 gagaagggtc ctactggaag cgaagggtgca gggcagcagg gcctgaggcg caggagctgg 240
 tggaggctcc cagcacagggt cgccgccccca gtcacatcac tgctgatggt ggggggactt 300
 ggggagtttc ccccgagaat gggagggtctc acagtccccg tgctgcaatg ctgtcgggtgc 360
 actgngncng caatgtgctc atggncactt gctttttctc tgtggccccg gccgatttat 420
 ccagcanngc accctctctc tncctctccg anaaagcc 458

273

<210> 746
 <211> 893
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(893)
 <223> n=A,T,C or G

<400> 746
 aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cgtggggagt tagctctctg 60
 gaccccgctca tagagtaagt catcgataga gcatttgctt gatggggact tccagaaggc 120
 canngaaagt cctgccgact tcctggggaa gcccatccgc acgtgggggtg agggccccca 180
 natggaagca gctgtgtatg cagggagggg gcagaggctg ctgccaatgg gcatgtccct 240
 tacctgaaag ggccacctct ccagggtgaca tgtcctgggg gagccggggc cgtctgctcc 300
 ggccagaggc gctcagctca ggccacacca ggccaggcac ctcccaacct ggacagggtg 360
 ggaccaagggt ggccttggac aaaactctct gtgtttgcca agcacccaat cggacacaga 420
 gagtcaacca caccacagtc acatggtgtc cacacngcag ggggtcaagga ggccccggccc 480
 ctccccctca gacgtccctg ggcctctggg agtcagcaag gacgaggacg gcatgtccct 540
 tcgagacagg aaggagagtga cctcctcccg gcggcatcca ggctcngctt ctccggagag 600
 gagagggggc tacttgctgg ataaancggc cggggccaca gagaaaaagc aaggtgacca 660
 tgagcacctt gcaaacacag tgcacccacc agcatttnag caccnnggac tgtgaagacc 720
 tcccatttct tcggggggaa acncgcccac ngttcccccc accntcacta gtgnattgtg 780
 acctgggggn cgggccgacc cctgtngctt gggnnagccc tccnccagg tttctnnggc 840
 ngcccnttaa nggnccctng nttggccctt tggcncctt tncgcttttc cca 893

<210> 747
 <211> 738
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(738)
 <223> n=A,T,C or G

<400> 747
 gatatcccg gaaattcgcg ccgcgtcnac gaagcacaga cctgngccct gctctcatgg 60
 ggcagactgc catttgtcat tnattactga aggaaggga tcctcagttt gcttgtggac 120
 atttcaaatt tgaggtgaga gttggataag taagaataaa gctgctcttc aaagagatga 180
 atatagaaa agaacaaga tacagncttg gcagtaaggc tgggaggaag gggaaaagg 240
 aataaagaat gaaagagtga gaaatgtgag caggagctga acacagaaaa gttcagngac 300
 agaagcanaa ggagggaaga agggaggagg gtccctttca cagaggctca cgaggatgct 360
 ttatgngtgc catgcagtcc atgttcagga tgtctgcttc ttanctctct acttttctaa 420
 tanaaatttg gatacttact gatcctacat atgtaacagg gagagaagg gaatttcaaa 480
 gcantaaatt gaaaaattgt tcacaatttc attttttaaa aaaaggagc taacagaaga 540
 agaggttaat gtggttaatta taggatgnct cttgcgcac atgaatgnat ctggtatcat 600
 ctgagtggga ggggagctgt cttcctgacc caaaaggatc ctttcgttan ccgnactta 660
 ngtcccaaaa cctcaccacc ttggagaaat natttccttt tgggggtntc attaaancct 720
 tttggncccc gcaaaagc

<210> 748
 <211> 647
 <212> DNA
 <213> Homo sapiens

<220>

274.

<221> misc_feature

<222> (1)...(647)

<223> n=A,T,C or G

<400> 748

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ctntgtggcg gtggctgtct catttgggtg gacttttttg gtcgtaggaa cctggtatng 60
aggtcgagag taagacgggc tattagtagt cgcacggag ttatttgtga aaacctggtt 120
agggcctctg tctccgctgc gctcgcctaa attggtatgg ctcgacttgg aaacacggtt 180
ctaacacgcg ttgttagcgc ccttgctagc atgtgaagga cactggccct accaagaaag 240
attcgagtcg ctccctcccg tatcggtcac ggaggcgata ttactcttc ttactacggt 300
tacttcgaga ttgtctgtga agtttaagac tactaaaaag agtattaagc ctatcgggaa 360
ttagctagat cgacacgcta aaaccaaggg caatcggcgg aaatatagag gcaccaataa 420
tagggcctac agaaggcccg agggtagac tcacgtttaa taccggccac gggagaaata 480
aaaagataaa gtatacatcg tttagcggtc ctcggaagcc ttcggcttta atgccaagga 540
gtcggaaagca tcgtcggcga gtaataaact ccatcgccgc gagactatct acgacgccct 600
ccttaanac cgtaaattac tcccggaaag agtatttagg cggctct 647
```

<210> 749

<211> 642

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(642)

<223> n=A,T,C or G

<400> 749

```
ctntgtggcg gtgngtgtct catttgggtg gacttttttg gtcgtaggaa cctggtatgc 60
aggtcgcgag agcgtgggct ctcgctgtgg atgttggggg ttggtgtggt gccggttgtt 120
tttggttctg ttgagcgtag tgtgtttgaa ggtagcgtt cgtgtcttgc ttgtggtttg 180
gtgttttagg cgggtgggga ggttgtttgt tagctgttgc atgtcatatt gttggtgttg 240
ctgccctgtg ctgtttgtcc ttggttattg tgggtgttac cccgcctgtg tggaagtgtt 300
gtggcagggc gggaatttaa gtgggagagt tgtgggaccc gtggttgttg ttacgttgc 360
gcttttgcg tgggcgggtg cggcgcgtct gataattaga attggatacg gagtgtataa 420
tacttctagt aaatggggac ctagtgttgc acttcccga atagggatct atgcgaagtc 480
cttaggatag tctttgataa gttaacgcc caccacccta aaattataca cgttagagac 540
cataacgact cctccaggaa agataaagaa tctcacatat agaacgggac cccatacacg 600
tcggatagga aacaagagaa ctaattttng ttaaaaagac tt 642
```

<210> 750

<211> 639

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(639)

<223> n=A,T,C or G

<400> 750

```
tttgtggcgg ttggtgtctca tttgggtgga tttttgggtc gtaggtaacc tgggtatngag 60
gtatagatgc cgattggtcc cgacgagcgt caccgataat tcggtagttt cgcccttttt 120
agaaggcgt agtactcgga acttcacttc atctcggtag ttacttttg cgtatatagc 180
cttctccctc gaagactagc cgtcacattc gttccctagg aatcgtttct gcccctaaga 240
atccgagagc gagatcccga aactagagga accttagaag agtcgtattt ccacaaggac 300
cccacagta ttccgggaaa atccctagga ccatacgggt aggattcccc cggaaccccg 360
agcaaagctc atgatttccc acaccgcgag agcgcctata accctatccc atttcttcgg 420
```

275

```
gttatcgagg atattacgat caagccgaga gaaccgctag aaccgctttc ttcgctttct 480
cacggaacct ataagtagaa agagaaactc aggtcttaag ggggcgcttc ggctaacgaa 540
actttctact acgaagagag tatctagaca ttaagtcata aaaatccact acgcacctcg 600
tgtacgatat catcgggagc ggttcataga cgggtgtccg 639
```

```
<210> 751
<211> 637
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(637)
<223> n=A,T,C or G
```

```
<400> 751
cttttgtggc ggnggtgtct catttgggtg gatttttggg tcgtaggnaa cctggtatng 60
aggcagctct gagccccccc ccccccccc ccccccnccc ccccccccta ggnggttggg 120
aanacgggtg atacctaaat cgagtgngtt cattaaaagt agttgattac nccctaaaaat 180
aanaanaggg cttcgtcggg anaaatcggg aagganaagt cttnttggca tcataanaat 240
actggctcgg gtcctaanaat nttaaggng gtcnccgagg gtnttcatac cgataanaaa 300
cgttttccta tcggcaacgg gcttacctga gggnggactt ctcnccgngc ggngattnan 360
acgaanacgt agaggattnc cgtacttnt tganatcacn cgtatcatac ttgtaagcat 420
aattntcctg aaaagtgtta taanaatacg cncgcataat cgcttttttcg tcctagggat 480
gcttaaatgg cgatactgct atagcgggtg agcgttggtt ctcgagnaana aaagcgtgtc 540
ctaattgcgtc taaggnttta agnecgttgg tttaaaaata nccttagaaa cctcgaggcg 600
gatactggtt tntttttaac gaaacaaagc accccnn 637
```

```
<210> 752
<211> 644
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(644)
<223> n=A,T,C or G
```

```
<400> 752
tntgtggcgg tgggtgctcat ttgggtggat ttttgggtcg taggaacctg gtatgaggtc 60
ttgcgagttg ttggtgtgtc ctgtcggttcg gtggttccct tttgagttga gtttgcctt 120
tgaggttgtt agctgctgtt cgtttgtgtt cgtgtagtgc tttgggttga gagggttatg 180
gtggtgggta cgggtgtattg tcgcccgtgg tcgcgggggtt ggggtgggtc tcggttttgt 240
ggttcatagt agtcttctgc gttcgggtgt gcggttttg gtgagtagtt tcgttcttgg 300
atgtcccatt gacccgccat aatctaagta agggtagta gaaacctctc cccgatatagac 360
acaaccgtcg tccactaaag acctcgctc tgatttttaa aaggaccgga aaaacatccc 420
ttcaacggaa aaaacggaaa aaaagtcagc gaattcaaag aagccacggg agagaaaaaa 480
gaactaaaagt tagtccgtca ttatatgtct cctcggagga ggaagcggcg gtggcggaaa 540
atgaggcggg aagaaagacg acctctatcg gcggttang ccctaaaagg gcgataacctt 600
acgggatgat aaggacccta ggacgcctcc ttctcggatc gtcc 644
```

```
<210> 753
<211> 635
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
```

276

<222> (1)...(635)
<223> n=A,T,C or G

<400> 753
ctttgtggcg gtggtgctca tttgggtgga tttttgggtc gtaggaacct ggtatgaggg 60
aatcagctcg accccccccc cccccccct ccgaagcaga gcccaaccca aagtcaccg 120
actaccgag taaactctcg gagggtagaa taagaaggag taggtcctag ccaatagaag 180
tagttccgag ccgttaggac agcggacgga acattnaaga aagagcctat attagggagg 240
aagtaacgtt cctctttcgg agctctttaa ggggtagtcc cagaacaagg gaagaggacc 300
cgtcggctat tgcccgtcga tacgggctct cacggngagc ctaggttcga ggatagggcc 360
gctcgtaaaa ttatacgggt tccgagaaac gcttccgtag accgggtcct aaatcgccg 420
gagtatnng agagggatcc ttcggaccct agggacagag agaggagaac ggaggttaca 480
ggaggagaac gnttcctcnc tagttttctt tangtcgaaa aatttcttac cgataggggt 540
cctagggctg gngaatttac gggtcgaaaa acggtagtnc ctaangngtg ntatnngggg 600
tagtatcggg tcgtttacaa ntgcgccgto ttntg 635

<210> 754
<211> 721
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(721)
<223> n=A,T,C or G

<400> 754
accggattng ttctgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagatcc cagtgggaga 360
cccctaaagc agaggagaa taaggagttc tccccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgtcttctt cccaccctc ttcccagct ctctctctgt 540
ctctctcttg ntccctgac ccttttttct tcccantgca tacttttttn ttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tcaccctga 660
ataggggatt cnttangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a 721

<210> 755
<211> 721
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(721)
<223> n=A,T,C or G

<400> 755
accggattng ttctgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagatcc cagtgggaga 360

277

```

cccctaaagc agagggagaa taaggagttc tcccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tcccactgc 480
gtgtacactt tatctgtctc ttgtcttctt cccacccctc tttccagct ctctctctgt 540
ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn tttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tcaccctga 660
ataggggatt cnttangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a 721

```

<210> 756

<211> 873

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(873)

<223> n=A,T,C or G

<400> 756

```

ggaagaatac agtaagtttg caaattaaaa tttctctatt tttctgttat ttattcattt 60
ggaaactgtc agcctgtctc ttccactttg ggcaagtga agcaaagacg tccagtccta 120
tcagcaatta ggctgaaagt caacgccaaag ctggcgggca agggctggtc tgagtagagg 180
ttccctagga aggaagaga gagactccca ctcgatactc ccagctcggc aactgcctga 240
atgccaatga gcactcatta taaccgccc tattttatag gatttaattt tacacttcag 300
gcttaatcag tctgaaagtt aaactgacag tgttaagtta cggaatcaat gacatttagg 360
ctttatgact ttgtagctga atatctatgg gctataattc cattctaaca gtgatacct 420
gttccagaat ctcatctctt ggtgatggca ctttctagtg gagcagtcac ggtaacagtc 480
cacaccatt accatgtggg tgctttacag catactgacg gaaggactga ggagccaccg 540
gagcaggagt tcctctcagg gaggacgctg acacttcac agctgcctan gtatgggcac 600
ctgatgccaa cgaanaaccc aaagcgctct cccttcaga tggagctgc cccacactgg 660
gctgacagca tctggagctg ctctggctca aatcccgaa tcgcacanct cctancgggg 720
gcgtttanag atcctcnggg ccagctaccg accacttttg acaagggnct taggagcgat 780
aactagnctg gcgcgttaca cncggatgga acgtcttgga cttgagacct cttgggggan 840
atggcncccc caaataantt gggaaaantn ggg 873

```

<210> 757

<211> 782

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(782)

<223> n=A,T,C or G

<400> 757

```

ggccccctga gggatactct agagcggccg ccgactagtg agctcgtcga cgatatcccg 60
ggatttgaga ccaggagaca gctccagatg ctgtcagccc agtgctgggg gcaggcttcc 120
atctgtgaag tggagaggcg ctttgggctt cttcgttggc atcagggtgc catacctagg 180
cgagctgtgg aagtgtcagc gtcctccctg agaggaactc ctgctccggt ggctcctcag 240
tccttcggtc agtatgctgt aaagcaccca catggtaatg ggtgnngact ggtaccatga 300
ctgntccctt aaaagggtggc cttccnaag aaaggagaat tcttggaacna gggatttcac 360
ttgnttagaa atgggaaaaa ttaccatta gaatttcgn ttccaaggcn tnaagncta 420
aaaggccttt gattcccgaa ccttaaccct gggcagttaa cctttcaaac gggataaacc 480
ctgangggga aatnaaatc ctttaaaaaa gggggggtt naaggagggc tctttggctt 540
tcaggcantt gccaacctgg gaaattcana ggggaagtnt tttttttgc ctgcctaggg 600
aacctttact taaacnaacc cttgncccc catttgggt tgactttcan cctaattgct 660
gaaaggaccg ggccgntttt gntttcctt gncccaaagg naaanaaacg ggtgccantt 720

```

278

cccangggat tanttcccga aaatttggnn aatttttntt tgnaactttt tgggtttttt 780
cc 782

<210> 758
<211> 647
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(647)
<223> n=A,T,C or G

<400> 758
ntttgtggcg gtggtgtctc atttgggtgg acttttttggg tcgtaggaac ctggtatnga 60
gggaagagcg ccgtcgggtcc gactacagta tggagtagta tagtcttcgc gccttctcgg 120
gcggcggggc tattctctcc aaaggcagag gtccctagtc gacctcgctc ccctaggtta 180
ggaacagccg tcgaatattt taggttcgtc gaggctttct tccgagctct acgcctaagt 240
agctccgcga gcaaagtatc ggtcattttc ccctatccat cactccccta agtacgcctc 300
attattcccg aaggcaagag gccagcattc ctcccttagag tagagggtag gtacctccgt 360
cgcgtgccgc gaaagggcag agcttcgtgt ctccctcccg cagcagctta acggtctacg 420
taggcgtttc cgatcttttc acgggaatcg gggtcgggga gggcggcgga aaacgtcgac 480
gtctcggtca ccgtcaccgc cccgaacaac tagcggcttt ccgctttcaa ctgaggaacc 540
ccgcacccct cattagcgtc tacgaaatcg gggangtgat tgcgccaatt cgtttagcctt 600
cgataattat tctctattag cgttcctatc tcgcgctttc gatattat 647

<210> 759
<211> 657
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(657)
<223> n=A,T,C or G

<400> 759
ctttgtggcg gtggtgtctc atttgggtgg acttttttggg tcgtaggaac ctggtatnga 60
gggctctata gaaagcctct tgtcttttaga tacgggcttt ctggtccttc gttctggaag 120
tgtagtagta ggtactgcgg gaaggcgaag agtcctttca aggacgattt acttaagttg 180
gcttatttct tagttccttc gggacataag gtcggtacga tctatactgc gtgggaagct 240
gataggtttg gacttaagga gaataagaag gaggcggcgg aggtcgcgat taccgcagag 300
atattattta cggcgccgcg ggttaccgcg ggtcatgcgg aaattttctg aggttcttgg 360
attcctaaga tcgctcccgt cgagtatact agcgacgaac gtaagagtgc cctcacaaga 420
accggtacaa actcaagaag aagttcccat taagcatcgt aagaaacggt aggacgagga 480
cggtagaaga taatcggaga aaggatccta gtngttacga agaagcatcg tttagctact 540
ttgcgctacc gtttatattt agacgtgttc cgtccttctc cgtgtttana aaaaaggttt 600
attccgacgg gagacttagg cgaatggagg gttccgcggg tganaatcgg ancgggg 657

<210> 760
<211> 644
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(644)
<223> n=A,T,C or G

279

<400> 760

```

ctttgtggcg gtggtgtctc atttgggtgg acttttttggg tcgtaggaac ctggtatgna 60
gaaaaagaag taagcctcga agcctatctc cgaccgtatt tatttcgcag aagacggaac 120
tacggacgtc gttaaccccg agtagccccc gtaagaaagg actaaagcga atggaaaagt 180
cgggaattcc ggcggaagggg cggcgattac tgaaaggagt aagagtaaga ctattgcgat 240
acttgaggcg ttccctctta aaaggcaccg gaaacactct attaaaaaac acccgaagaa 300
gaacaactca tgcgatcggc cgtgtgcagc cgtcaatagt aaagagagcc atgaaccatg 360
ccatccttag accaattagg atgaagaaga ggagggaagt gaggaccaa ccctaccac 420
tcggaaaacc ccgcacgagc ctccgaacaa aatccgggaa ttaaaacggc ggcccacttc 480
cgcactctcg tagcgcgagc cgaatagaaa accggaact acagctaaag ggtcctttcc 540
ggcctgttat ctaccacccc gcaatccgat cctccccccc cctcgtccaa aaaccctaac 600
ctctgcggca acattagagc agaaggagag ggcgatccct tgan 644

```

<210> 761

<211> 647

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(647)

<223> n=A,T,C or G

<400> 761

```

ctttgtggcg gtggtgtctc atttgggtgg acttttttggg tcgtaggaac ctggtatnga 60
ggcgggtact ctctgggata atcgggtataa gtgttgtaaa attgggggta agagaaagt 120
tcattataag aagtgggaagc acgagccggg gtgttttagtc gttaatatta agaccggtt 180
ttgttgtagt tatatagctt gcgcgtgggg aggcaataag aaacattgcy tttcgaggcc 240
ggatgcgggg aaccctcttc ggggtctaga gcgcgcgcatc tgcaaaataa ggactactga 300
cgcgcgtcat aacgtactca acaatgagtc ggcctgcatt aagattttcg cgaagaaccg 360
tactgcgtct actgatagta tattgcattg atagcggcat gagctttatc acgtgtcgtt 420
ttcgggttgt aagaaggag ttaagtcgat cttcgaggaa gaagagacc caaataaaaa 480
atgactcaaa aaaacctaga agaaacacga cgaaaggaaa aagaacgtta aaactagtag 540
ctcttcggan gagtagcctt agtagggtaa gtcctccgtg cgtactgtcc taaggtttgg 600
atagcgcggt tgaatagacg gtcacgcgtc agaaggtaaa aancgg 647

```

<210> 762

<211> 628

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(628)

<223> n=A,T,C or G

<400> 762

```

cattgtgttg gggtcactga gccactttt ttccagattt tttgtaaaat tgtttcgcat 60
tgtgttccct ttattcgctt gtattaatat ttgcgtagtg gattaaacaa atacttggtg 120
ttgactgtca gtcttagagg actgactaga agtagttttc atttggggct caggaaatac 180
ctactttata tttctagcta attaggaaag tcatttttca gttagggttg tgttttggtt 240
caggcactcg ctagctagat gacctaacat gctacttaat ttctgagtgt ttgtgtccat 300
ccctgtagga ttgttgcggt gttaaatgaa atttgttata tttgtaaaag atttacctca 360
gtgcccagac tgtgacagag tagattatta ggcttgcctt tatttctgtg attaaattta 420
gtgtcagatt agcaacctat agctacttct aaagctgctg ctgctttctt tgtttagggt 480
taggaagaaa catgctggac agtttgccaa atgagagtta catgatgttg cttgtgggaa 540
cattctaact tggaacttgc ccattttccag gactttgnng ttcanagatt tttggggata 600

```


280

gatgtaaggg ttataaaaaa cngaaaac

628

<210> 763

<211> 147

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(147)

<223> n=A,T,C or G

<400> 763

cattgtgttg gggcagagat aaataattcc tctgaaaagt gttttattgg aatttcaaat 60
gaaaagctaa ctggataact tacagcatgt ttctgccaat aatctcttan aacaggcctc 120
ttttttttat gcacaccacc ttcnggc 147

<210> 764

<211> 146

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(146)

<223> n=A,T,C or G

<400> 764

cattgtgttg ggtatgtttt ttgaaggcag gtggacagga ttgctgatg ggtaaatggc 60
agagtttagg ggactgttag aacagagaaa.ganatcatgg ggttgggtt gagtctgatg 120
nnnaactggt gccgnntgct cagtat 146

<210> 765

<211> 129

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(129)

<223> n=A,T,C or G

<400> 765

tncncgattc gntnctagcg tntacactna tgtcttggtta ccgagctcgg atccactagt 60
ccagtgtggg nggaattcca ttgtgttggg gcaggaggng ctttnggtac ngtgcggctg 120
nagaggcgg 129

<210> 766

<211> 175

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(175)

<223> n=A,T,C or G

<400> 766

281

```

cattgtgttg ggcctagtc gaatactttt agtaacttca gacagatctc ctcactctctt 60
tctggggcctt ggnnttttctc ctttgtanaa tgatgccttt ctgtgggtttt gtcattttcta 120
acattctgtg ngtgatgagg tgtatatctg angancctcta tcnccanagt actct 175

```

```

<210> 767
<211> 602
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(602)
<223> n=A,T,C or G

```

```

<400> 767
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cctgggtttgt tttcagtggt taatcctatt agtatcagca ggatataggt caggatatca 120
ggtgcagaac ctgtggaatc agccaatttg gcttgctcat ttactttaat aagggtcccat 180
aatgagttag agtacaaagt tcaagccctg ttgagggctc gcattaaact ctcagaagta 240
tttagagtgt gccaggagcc gcgaaggctc gggtcgggtg gtggcgggaa ctgtattaga 300
gtgctaggca cggcgcgaca aagtctgtcc aacccaaaac ggtgctgagg cgttgggtgt 360
gagctccagt actcagaaaa gcactctcagc aggtactcaa cagatcctca ggggcttggg 420
ggcccagcac tggcagtgag ggcatgaaag acataaaaag gcactacctg tgggtatttt 480
ctgtttctcca aggaggaagt agcaaaaatt aggacgctgg aatatcctat gttgtagcaa 540
tcccagaaca actgatgctc aacaaatacc acacaaaaca aattttttaa aatttaactc 600
ta 602

```

```

<210> 768
<211> 671
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(671)
<223> n=A,T,C or G

```

```

<400> 768
tccaccgcgg tggcggccgc tctagactag tggatccact agtccagtgt ggggtgggaat 60
tcgcggcncg cgtcgacaaa aatactgcta aagtaatat tttatagatg actatttgcc 120
ttggggccag gaaaagcagc tggagttatt cacttagtac catTTTTTaca tactaaacttt 180
gcctttttcca tgcttgcttg atgcggcttg cagcactgaa gaacagtttc aattgctagc 240
caaccagaga gcatgatcaa accaaacaag ttccctgttt caggaaaaac aggttttagg 300
taactgaagg gttaccagtt actgattcca caatcttctc tgtaaaanat ttctgcctat 360
tatgcagact gggcggcttt aaanntggta aaactatnaa ataccatac aatattttta 420
nggggccccn ttatnaagct tttcaggcct tcccctttcc atagcattgg tgggatacaa 480
gaaaccttta aacagcaacn agctatcnag gcccaaaagg aaagtaattn tgatttttta 540
nagattccgn aacgaaaaaa tggctgggtt caaatacnac cttcttttta aaatggnttc 600
cttattaaac ntTTTTTTTT ttttaatttta ccccatggtc ntgatnttng ngcttccgcc 660
canaaaatng n 671

```

```

<210> 769
<211> 877
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

282

<222> (1)...(877)
 <223> n=A,T,C or G

<400> 769
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 ngggggaatt cgcggccgcg tcgacctcta tacctttgnt catgcagctt cctctgactg 120
 ggtttgttct tcaattggct aaccctctt ttacttaagc acaccttgaa cattccctcc 180
 ttccccattt ccccgagng ccctaattgg acatacttct gaataacaca ggtggtattc 240
 cttccttggt ggaacctcct ggaggaagag acagatgatt aacaaatcct tccatcaacc 300
 cctttgacca tgacatcaac agtgctccaa attatggggg accgtattag cctatgtcta 360
 tcctgatcag aatccttacc tcgggtgtatt gaaattatct atttcgtgcc tgcctcttta 420
 aagtcagggt ttgccttattc tattgtctaa caccatgcag taggtaacat gcagtaggaa 480
 acatggcatt aaattatttg ggttcaaata ccagttatgg tgtgtaaatg cctaccaggc 540
 cgtgaggcac ctgctaagca ggttgacgc atcatttgaa ttcacaccac ccttttgcaa 600
 tagaacagat aggaacacaga ggctcatttg ggctaagga ttgatggag ggaagtgcc 660
 aggattccca ccaaggcctc anggccagg tccanggacc atgtctgttg tgacaactgg 720
 agtgcatttc atatccctn ctctgngggg naaggtccct cncgnggaga acnnttaaaa 780
 caatcatntc tnggggngnt aatgcttctt nccccagtg ggtncactgc ngccacgagt 840
 cccanccact agtcccangt ctgtcatgaa ccancce 877

<210> 770
 <211> 874
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(874)
 <223> n=A,T,C or G

<400> 770
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 gaattcgagg cgcgctcgac cttttcaaag gttaacttat ttaattatca canngcaac 120
 ccgatgagta ggtaacagta ttttactgat aggtaatcta aagaaggagg ctaaataaat 180
 tgcccaattt cgaacagtga gaggaagaat taggattgaa acacatatag tggcttcaga 240
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 tgttcctatg tcatcaaatt atacttactt taaaaagtat ttgtctttat tattttttaa 360
 aaaacacagg gaagtatttc tgatcagggg cagtattggg tctgaaagac aagccagtgt 420
 ttttgagggt ttctoccttg ccagtttttc tatgctgggt tattcaagtc ctaagaattg 480
 tgtagctatt acagaaccgc tttagcaaata gtgttccatt aatcaagggt atttataaca 540
 aaatttcata caagtttgga gtgctctgaa aacatagcca aaatgttcgc agggctacc 600
 cctctcgtgt gtcccttttt tttagctatt tcagaagcac actggtgcaa tattttacga 660
 aatgagtttc ttccctttac ctctgcatcc tctaagaaaa aatcattgnt gttttatgaa 720
 natgaanata ctgctatttc atatcttgat tggagctgct taattaaatg accattttta 780
 aatttgtttt gattccnngc aaaaaaagtt tnttnttgga tgtagggggc tcnnaaagnc 840
 caaaaccccc caaaattttt nnttggaac ccna 874

<210> 771
 <211> 156
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(156)
 <223> n=A,T,C or G

<400> 771

283

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ttaaaaaanct ggnctccccg cgggtggcggc cgctctagaa ctagtggatc cactagtcca 60
gtgtgggtgga attcgcggcc gcgtcgaccg cgagcggtcg cccttttttt tttttttttt 120
ngtttttttg aanaattcat tgggtattta ttattc 156

```

<210> 772

<211> 586

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)... (586)

<223> n=A,T,C or G

<400> 772

```

ncaanctggn ctccaccgcg gtggcggcggc ctctagacta gtggatccac tagtccagtg 60
tgggtggaatt cgcgcccgcg tcgatcacaa agtgctcaca agtccngnat ttattttatc 120
tccagatatg aaacttaccc ccagctatgg tottctatct gttatttaat ttctaggcca 180
attttttcca cttgaatgtc agtattttta ttcaaagtca ccttggtccaa ataccaagtc 240
atcaacttac cotcaaatca tatcctcatt cagaaaaatc acatctatta atggtagcta 300
ttttatccct gccccctgct ttttcttttt atattttaatt aatttgntca tccagcaaatt 360
gcttattgag caggtattgt aggcataaaca attctanact ttaaggggac acagnttgca 420
aaacaaaatc ctgccttgna tggatactta tgnnatggng ggatacagac aatcaacata 480
atgangngca tcatatataa tggttagnan aatgataagg gnttttgga aaaaaatgca 540
cccanccaan anggattggg aagtggangg ganggtcang ggangg 586

```

<210> 773

<211> 2983

<212> DNA

<213> Homo sapiens

<400> 773

```

agagatagag tcttccctgg cattgcagga gagaatctga agggatgatg gatgcatcaa 60
aagagctgca agttctccac attgacttct tgaatcagga caacgcggtt tctcaccaca 120
catggggagt ccaaacgagc agtcctgtgt tccggcgagg acaggtgttt cacctgcggc 180
tgggtgctgaa ccagcccta caatcctacc accaactgaa actggaattc agcacagggc 240
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actacaactg gcaggcaacc ctcaaaaatg agtctggcaa agaggtcaca gtggctgtca 360
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tccttaagtc tgaagaaaac atcctatacc ttctcttcaa ccatggtgt aaagaggaca 480
tggttttcat gcctgatgag gacgagcgca aagagtacat cctcaatgac acgggctgcc 540
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```

```

actctgttaa tttcaccgtg attcttaaaaa ggaagaccgc tgccttacag aatgtcaaca 1560
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```

<210> 774

<211> 3064

<212> DNA

<213> Homo sapiens

<400> 774

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aattctaaaa atgcttttgc aagcttgcat gcctgcaggt gcagcgcccg ccagtgtgat 60
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285

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tacaatcaga tgatgtgctg ctgggaaact ctgttaattt caccgtgatt cttaaaagga 1620
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```

<210> 775

<211> 684

<212> PRT

<213> Homo sapiens

<400> 775

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Met Met Asp Ala Ser Lys Glu Leu Gln Val Leu His Ile Asp Phe Leu
      5              10              15
Asn Gln Asp Asn Ala Val Ser His His Thr Trp Glu Phe Gln Thr Ser
      20              25              30
Ser Pro Val Phe Arg Arg Gly Gln Val Phe His Leu Arg Leu Val Leu
      35              40              45
Asn Gln Pro Leu Gln Ser Tyr His Gln Leu Lys Leu Glu Phe Ser Thr
      50              55              60
Gly Pro Asn Pro Ser Ile Ala Lys His Thr Leu Val Val Leu Asp Pro
      65              70              75              80
Arg Thr Pro Ser Asp His Tyr Asn Trp Gln Ala Thr Leu Gln Asn Glu
      85              90              95
Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile
      100             105             110
Leu Gly Lys Tyr Gln Leu Asn Val Lys Thr Gly Asn His Ile Leu Lys
      115             120             125
Ser Glu Glu Asn Ile Leu Tyr Leu Leu Phe Asn Pro Trp Cys Lys Glu
      130             135             140
Asp Met Val Phe Met Pro Asp Glu Asp Glu Arg Lys Glu Tyr Ile Leu
      145             150             155             160
Asn Asp Thr Gly Cys His Tyr Val Gly Ala Ala Arg Ser Ile Lys Cys
      165             170             175
Lys Pro Trp Asn Phe Gly Gln Phe Glu Lys Asn Val Leu Asp Cys Cys
      180             185             190
Ile Ser Leu Leu Thr Glu Ser Ser Leu Lys Pro Thr Asp Arg Arg Asp

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286

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Pro Val Leu Val Cys Arg Ala Met Cys Ala Met Met Ser Phe Glu Lys		
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Gly Gln Gly Val Leu Ile Gly Asn Trp Thr Gly Asp Tyr Glu Gly Gly		
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Thr Ala Pro Tyr Lys Trp Thr Gly Ser Ala Pro Ile Leu Gln Gln Tyr		
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Tyr Asn Thr Lys Gln Ala Val Cys Phe Gly Gln Cys Trp Val Phe Ala		
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Gly Ile Leu Thr Thr Val Leu Arg Ala Leu Gly Ile Pro Ala Arg Ser		
275	280	285
Val Thr Gly Phe Asp Ser Ala His Asp Thr Glu Arg Asn Leu Thr Val		
290	295	300
Asp Thr Tyr Val Asn Glu Asn Gly Lys Lys Ile Thr Ser Met Thr His		
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Asp Ser Val Trp Asn Phe His Val Trp Thr Asp Ala Trp Met Lys Arg		
325	330	335
Pro Asp Leu Pro Lys Gly Tyr Asp Gly Trp Gln Ala Val Asp Ala Thr		
340	345	350
Pro Gln Glu Arg Ser Gln Gly Val Phe Cys Cys Gly Pro Ser Pro Leu		
355	360	365
Thr Ala Ile Arg Lys Gly Asp Ile Phe Ile Val Tyr Asp Thr Arg Phe		
370	375	380
Val Phe Ser Glu Val Asn Gly Asp Arg Leu Ile Trp Leu Val Lys Met		
385	390	395
Val Asn Gly Gln Glu Glu Leu His Val Ile Ser Met Glu Thr Thr Ser		
405	410	415
Ile Gly Lys Asn Ile Ser Thr Lys Ala Val Gly Gln Asp Arg Arg Arg		
420	425	430
Asp Ile Thr Tyr Glu Tyr Lys Tyr Pro Glu Gly Ser Ser Glu Glu Arg		
435	440	445
Gln Val Met Asp His Ala Phe Leu Leu Leu Ser Ser Glu Arg Glu His		
450	455	460
Arg Arg Pro Val Lys Glu Asn Phe Leu His Met Ser Val Gln Ser Asp		
465	470	475
Asp Val Leu Leu Gly Asn Ser Val Asn Phe Thr Val Ile Leu Lys Arg		
485	490	495
Lys Thr Ala Ala Leu Gln Asn Val Asn Ile Leu Gly Ser Phe Glu Leu		
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Gln Leu Tyr Thr Gly Lys Lys Met Ala Lys Leu Cys Asp Leu Asn Lys		
515	520	525
Thr Ser Gln Ile Gln Gly Gln Val Ser Glu Val Thr Leu Thr Leu Asp		
530	535	540
Ser Lys Thr Tyr Ile Asn Ser Leu Ala Ile Leu Asp Asp Glu Pro Val		
545	550	555
Ile Arg Gly Phe Ile Ile Ala Glu Ile Val Glu Ser Lys Glu Ile Met		
565	570	575
Ala Ser Glu Val Phe Thr Ser Phe Gln Tyr Pro Glu Phe Ser Ile Glu		
580	585	590
Leu Pro Asn Thr Gly Arg Ile Gly Gln Leu Leu Val Cys Asn Cys Ile		
595	600	605
Phe Lys Asn Thr Leu Ala Ile Pro Leu Thr Asp Val Lys Phe Ser Leu		
610	615	620
Glu Ser Leu Gly Ile Ser Ser Leu Gln Thr Ser Asp His Gly Thr Val		
625	630	635
Gln Pro Gly Glu Thr Ile Gln Ser Gln Ile Lys Cys Thr Pro Ile Lys		
645	650	655
Thr Gly Pro Lys Lys Phe Ile Val Lys Leu Ser Ser Lys Gln Val Lys		

287

660
 Glu Ile Asn Ala Gln Lys Ile Val Leu Ile Thr Lys
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<210> 776

<211> 679

<212> PRT

<213> Homo sapiens

<400> 776

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 Ser Pro Val Phe Arg Arg Gly Gln Val Phe His Leu Arg Leu Val Leu
 35 40 45
 Asn Gln Pro Leu Gln Ser Tyr His Gln Leu Lys Leu Glu Phe Ser Thr
 50 55 60
 Gly Pro Asn Pro Ser Ile Ala Lys His Thr Leu Val Val Leu Asp Pro
 65 70 75 80
 Arg Thr Pro Ser Asp His Tyr Asn Trp Gln Ala Thr Leu Gln Asn Glu
 85 90 95
 Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile
 100 105 110
 Leu Gly Lys Tyr Gln Leu Asn Val Lys Thr Gly Asn His Ile Leu Lys
 115 120 125
 Ser Glu Glu Asn Ile Leu Tyr Leu Leu Phe Asn Pro Trp Cys Lys Glu
 130 135 140
 Asp Met Val Phe Met Pro Asp Glu Asp Glu Arg Lys Glu Tyr Ile Leu
 145 150 155 160
 Asn Asp Thr Gly Cys His Tyr Val Gly Ala Ala Arg Ser Ile Lys Cys
 165 170 175
 Lys Pro Trp Asn Phe Gly Gln Phe Glu Lys Asn Val Leu Asp Cys Cys
 180 185 190
 Ile Ser Leu Leu Thr Glu Ser Ser Leu Lys Pro Thr Asp Arg Arg Asp
 195 200 205
 Pro Val Leu Val Cys Arg Ala Met Cys Ala Met Met Ser Phe Glu Lys
 210 215 220
 Gly Gln Gly Val Leu Ile Gly Asn Trp Thr Gly Asp Tyr Glu Gly Gly
 225 230 235 240
 Thr Ala Pro Tyr Lys Trp Thr Gly Ser Ala Pro Ile Leu Gln Gln Tyr
 245 250 255
 Tyr Asn Thr Lys Gln Ala Val Cys Phe Gly Gln Cys Trp Val Phe Ala
 260 265 270
 Gly Ile Leu Thr Thr Val Leu Arg Ala Leu Gly Ile Pro Ala Arg Ser
 275 280 285
 Val Thr Gly Phe Asp Ser Ala His Asp Thr Glu Arg Asn Leu Thr Val
 290 295 300
 Asp Thr Tyr Val Asn Glu Asn Gly Glu Lys Ile Thr Ser Met Thr His
 305 310 315 320
 Asp Ser Val Trp Asn Phe His Val Trp Thr Asp Ala Trp Met Lys Arg
 325 330 335
 Pro Tyr Asp Gly Trp Gln Ala Val Asp Ala Thr Pro Gln Glu Arg Ser
 340 345 350
 Gln Gly Val Phe Cys Cys Gly Pro Ser Pro Leu Thr Ala Ile Arg Lys
 355 360 365
 Gly Asp Ile Phe Ile Val Tyr Asp Thr Arg Phe Val Phe Ser Glu Val
 370 375 380

288

Asn Gly Asp Arg Leu Ile Trp Leu Val Lys Met Val Asn Gly Gln Glu
 385 390 395 400
 Glu Leu His Val Ile Ser Met Glu Thr Thr Ser Ile Gly Lys Asn Ile
 405 410 415
 Ser Thr Lys Ala Val Gly Gln Asp Arg Arg Arg Asp Ile Thr Tyr Glu
 420 425 430
 Tyr Lys Tyr Pro Glu Gly Ser Ser Glu Glu Arg Gln Val Met Asp His
 435 440 445
 Ala Phe Leu Leu Leu Ser Ser Glu Arg Glu His Arg Gln Pro Val Lys
 450 455 460
 Glu Asn Phe Leu His Met Ser Val Gln Ser Asp Asp Val Leu Leu Gly
 465 470 475 480
 Asn Ser Val Asn Phe Thr Val Ile Leu Lys Arg Lys Thr Ala Ala Leu
 485 490 495
 Gln Asn Val Asn Ile Leu Gly Ser Phe Glu Leu Gln Leu Tyr Thr Gly
 500 505 510
 Lys Lys Met Ala Lys Leu Cys Asp Leu Asn Lys Thr Ser Gln Ile Gln
 515 520 525
 Gly Gln Val Ser Glu Val Thr Leu Thr Leu Asp Ser Lys Thr Tyr Ile
 530 535 540
 Asn Ser Leu Ala Ile Leu Asp Asp Glu Pro Val Ile Arg Gly Phe Ile
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 Ile Ala Glu Ile Val Glu Ser Lys Glu Ile Met Ala Ser Glu Val Phe
 565 570 575
 Thr Ser Asn Gln Tyr Pro Glu Phe Ser Ile Glu Leu Pro Asn Thr Gly
 580 585 590
 Arg Ile Gly Gln Leu Leu Val Cys Asn Cys Ile Phe Lys Asn Thr Leu
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 Ala Ile Pro Leu Thr Asp Val Lys Phe Ser Leu Glu Ser Leu Gly Ile
 610 615 620
 Ser Ser Leu Gln Thr Ser Asp His Gly Thr Val Gln Pro Gly Glu Thr
 625 630 635 640
 Ile Gln Ser Gln Ile Lys Cys Thr Pro Ile Lys Thr Gly Pro Lys Lys
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 Phe Ile Val Lys Leu Ser Ser Lys Gln Val Lys Glu Ile Asn Ala Gln
 660 665 670
 Lys Ile Val Leu Ile Thr Lys
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<210> 777

<211> 5668

<212> DNA

<213> Homo sapiens

<400> 777

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<210> 778

<211> 1095

<212> PRT

<213> Homo sapiens

<400> 778

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Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
      35              40              45
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
      50              55              60
Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
      65              70              75              80
Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
      85              90              95
Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
      100             105             110
Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
      115             120             125
His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
      130             135             140
Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
      145             150             155             160
Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
      165             170             175
Tyr Gly Leu Thr Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
      180             185             190
Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
      195             200             205

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291

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 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
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 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Val Asp Asn
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 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
 260 265 270
 Glu Lys His Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
 275 280 285
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
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 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
 305 310 315 320
 Glu Gly Ser Gly Arg Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
 325 330 335
 Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
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 Leu Pro Arg Thr Val Ser Arg Leu Ser Glu Glu Glu Thr Glu Ser Trp
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 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
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 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
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 405 410 415
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
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 485 490 495
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
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 565 570 575
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 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
 595 600 605
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
 610 615 620
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
 625 630 635 640
 Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp
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 Gln His Phe Thr Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
 660 665 670

292

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
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 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
 690 695 700
 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
 705 710 715 720
 Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
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 Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
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 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
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 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
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 995 1000 1005
 Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
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<212> DNA

<213> Homo sapiens

<400> 779

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294

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<210> 780

<211> 1095

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> (1)...(1095)

<223> Xaa = Any Amino Acid

<400> 780

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                    35              40              45
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
                    50              55              60
Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
                    65              70              75
Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
                    85              90              95
Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
                    100             105             110
Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
                    115             120             125
His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
                    130             135             140
Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
                    145             150             155
Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
                    165             170             175
Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
                    180             185             190
Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
                    195             200             205
Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
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Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
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Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
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Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
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Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
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				340	345						350				
Leu	Pro	Arg	Thr	Val	Ser	Arg	Leu	Pro	Glu	Glu	Glu	Thr	Glu	Ser	Trp
				355	360						365				
Ile	Lys	Trp	Leu	Lys	Glu	Ile	Leu	Glu	Cys	Ser	His	Leu	Leu	Thr	Val
				370	375						380				
Ile	Lys	Met	Glu	Glu	Ala	Gly	Asp	Glu	Ile	Val	Ser	Asn	Ala	Ile	Ser
				385	390						395				
Tyr	Ala	Leu	Tyr	Lys	Ala	Phe	Ser	Thr	Ser	Glu	Gln	Asp	Lys	Asp	Asn
				405	410						415				
Trp	Asn	Gly	Gln	Leu	Lys	Leu	Leu	Leu	Glu	Trp	Asn	Gln	Leu	Asp	Leu
				420	425						430				
Ala	Asn	Asp	Glu	Ile	Phe	Thr	Asn	Asp	Arg	Arg	Trp	Glu	Ser	Ala	Asp
				435	440						445				
Leu	Gln	Glu	Val	Met	Phe	Thr	Ala	Leu	Ile	Lys	Asp	Arg	Pro	Lys	Phe
				450	455						460				
Val	Arg	Leu	Phe	Leu	Glu	Asn	Gly	Leu	Asn	Leu	Arg	Lys	Phe	Leu	Thr
				465	470						475				
His	Asp	Val	Leu	Thr	Glu	Leu	Phe	Ser	Asn	His	Phe	Ser	Thr	Leu	Val
				485	490						495				
Tyr	Arg	Asn	Leu	Gln	Ile	Ala	Lys	Asn	Ser	Tyr	Asn	Asp	Ala	Leu	Leu
				500	505						510				
Thr	Phe	Val	Trp	Lys	Leu	Val	Ala	Asn	Phe	Arg	Arg	Gly	Phe	Arg	Lys
				515	520						525				
Glu	Asp	Arg	Asn	Gly	Arg	Asp	Glu	Met	Asp	Ile	Glu	Leu	His	Asp	Val
				530	535						540				
Ser	Pro	Ile	Thr	Arg	His	Pro	Leu	Gln	Ala	Leu	Phe	Ile	Trp	Ala	Ile
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Leu	Gln	Asn	Lys	Lys	Glu	Leu	Ser	Lys	Val	Ile	Trp	Glu	Gln	Thr	Arg
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Gly	Cys	Thr	Leu	Ala	Ala	Leu	Gly	Ala	Ser	Lys	Leu	Leu	Lys	Thr	Leu
				580	585						590				
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Trp	Tyr	Gly	Glu	Ile	Ser	Arg	Asp	Thr	Lys	Asn	Trp	Lys	Ile	Ile	Leu
				675	680						685				
Cys	Leu	Phe	Ile	Ile	Pro	Leu	Val	Gly	Cys	Gly	Phe	Val	Ser	Phe	Arg
				690	695						700				
Lys	Lys	Pro	Val	Asp	Lys	His	Lys	Lys	Leu	Leu	Trp	Tyr	Tyr	Val	Ala
				705	710						715				
Phe	Phe	Thr	Ser	Pro	Phe	Val	Val	Phe	Ser	Trp	Asn	Val	Val	Phe	Tyr
				725	730						735				
Ile	Ala	Phe	Leu	Leu	Leu	Phe	Ala	Tyr	Val	Leu	Leu	Met	Asp	Phe	His
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296

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785      790      795      800
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      805      810      815
Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
      820      825      830
Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
      835      840      845
Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
      850      855      860
Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865      870      875      880
Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
      885      890      895
Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
      900      905      910
Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
      915      920      925
Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
      930      935      940
Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945      950      955      960
Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
      965      970      975
Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
      980      985      990
Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
      995      1000      1005
Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
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      1060      1065      1070
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<210> 803
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<210> 804

<211> 15

<212> PRT

<213> Homo sapiens

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aaagagactt	tgaagccat	caatacctcc	atcaaaaata	aaattccttg	tgtggtggtg	960
gaaggctcgg	gccagatcgc	tgatgtgatc	gctagctctg	tggaggtgga	ggatgccctg	1020
acatcttctg	cgctcaagga	gaagctgggt	cgcttttttc	cccgcacggt	gtccccgctg	1080
octgaggagg	agctgagag	tggatcaaaa	tggctcaaac	aaattctcga	atgttctcac	1140
ctattaacag	ttattaaaat	tggaagaagct	gggatgaaa	ttgtgagcaa	tgccatctcc	1200
tacgtcttat	acaaagcctt	cagcaccagt	gagcaagaca	aggataactg	gaatgggcag	1260
ctgaagcttc	tgctggagtg	gaaccagctg	gacttagcca	atgatgagat	tttcaccaat	1320
gaccgccgat	gggagttctg	tgaaccttcaa	gaagtcatgt	ttacggctct	cataaaggac	1380
agacccaagt	ttgtccgcct	ctttctggag	aattggcttga	acctacggaa	gtttctcacc	1440
catgatgtcc	tcactgaact	cttctccaac	cacttcagca	cgcttgtgta	ccggaatctg	1500

303

cagatcgcca agaattccta taatgatgcc ctctcacgt ttgtctggaa actggttgcg 1560
 aacttccgaa gaggttccg gaaggaagac agaaatggcc gggacgagat ggacatagaa 1620
 ctccacgacg tgtctoctat tactcggcac cccctgcaag ctctcttcat ctgggccatt 1680
 cttcagaata agaaggaact ctccaaagtc atttgggagc agaccagggg ctgcactctg 1740
 gcagccctgg gagccagcaa gcttctgaag actctggcca aagtgaagaa cgacatcaat 1800
 gctgctgggg agtccgagga gctggctaag gactacgaga cccgggctgt tgagctgttc 1860
 actgagtgtt acagcagcga tgaagacttg gcagaacagc tgctggtcta ttcctgtgaa 1920
 gcttgggggtg gactcgagca ccaccaccac caccactga 1959

<210> 818

<211> 652

<212> PRT

<213> Homo sapiens

<400> 818

Met	Arg	Asn	Arg	Arg	Asn	Asp	Thr	Leu	Asp	Ser	Thr	Arg	Thr	Leu	Tyr
				5					10					15	
Ser	Ser	Ala	Ser	Arg	Ser	Thr	Asp	Leu	Ser	Tyr	Ser	Glu	Ser	Asp	Leu
			20					25					30		
Val	Asn	Phe	Ile	Gln	Ala	Asn	Phe	Lys	Lys	Arg	Glu	Cys	Val	Phe	Phe
		35					40					45			
Thr	Lys	Asp	Ser	Lys	Ala	Thr	Glu	Asn	Val	Cys	Lys	Cys	Gly	Tyr	Ala
	50					55					60				
Gln	Ser	Gln	His	Met	Glu	Gly	Thr	Gln	Ile	Asn	Gln	Ser	Glu	Lys	Trp
	65				70					75					80
Asn	Tyr	Lys	Lys	His	Thr	Lys	Glu	Phe	Pro	Thr	Asp	Ala	Phe	Gly	Asp
				85					90					95	
Ile	Gln	Phe	Glu	Thr	Leu	Gly	Lys	Lys	Gly	Lys	Tyr	Ile	Arg	Leu	Ser
			100					105					110		
Cys	Asp	Thr	Asp	Ala	Glu	Ile	Leu	Tyr	Glu	Leu	Leu	Thr	Gln	His	Trp
		115					120					125			
His	Leu	Lys	Thr	Pro	Asn	Leu	Val	Ile	Ser	Val	Thr	Gly	Gly	Ala	Lys
	130					135					140				
Asn	Phe	Ala	Leu	Lys	Pro	Arg	Met	Arg	Lys	Ile	Phe	Ser	Arg	Leu	Ile
	145				150					155					160
Tyr	Ile	Ala	Gln	Ser	Lys	Gly	Ala	Trp	Ile	Leu	Thr	Gly	Gly	Thr	His
			165					170						175	
Tyr	Gly	Leu	Met	Lys	Tyr	Ile	Gly	Glu	Val	Val	Arg	Asp	Asn	Thr	Ile
		180					185					190			
Ser	Arg	Ser	Ser	Glu	Glu	Asn	Ile	Val	Ala	Ile	Gly	Ile	Ala	Ala	Trp
		195				200					205				
Gly	Met	Val	Ser	Asn	Arg	Asp	Thr	Leu	Ile	Arg	Asn	Cys	Asp	Ala	Glu
	210					215					220				
Gly	Tyr	Phe	Leu	Ala	Gln	Tyr	Leu	Met	Asp	Asp	Phe	Thr	Arg	Asp	Pro
	225				230					235					240
Leu	Tyr	Ile	Leu	Asp	Asn	Asn	His	Thr	His	Leu	Leu	Leu	Val	Asp	Asn
			245						250					255	
Gly	Cys	His	Gly	His	Pro	Thr	Val	Glu	Ala	Lys	Leu	Arg	Asn	Gln	Leu
		260					265						270		
Glu	Lys	Tyr	Ile	Ser	Glu	Arg	Thr	Ile	Gln	Asp	Ser	Asn	Tyr	Gly	Gly
		275					280					285			
Lys	Ile	Pro	Ile	Val	Cys	Phe	Ala	Gln	Gly	Gly	Gly	Lys	Glu	Thr	Leu
		290					295				300				
Lys	Ala	Ile	Asn	Thr	Ser	Ile	Lys	Asn	Lys	Ile	Pro	Cys	Val	Val	Val
	305				310					315					320
Glu	Gly	Ser	Gly	Gln	Ile	Ala	Asp	Val	Ile	Ala	Ser	Leu	Val	Glu	Val
			325					330					335		
Glu	Asp	Ala	Leu	Thr	Ser	Ser	Ala	Val	Lys	Glu	Lys	Leu	Val	Arg	Phe

304

```

      340      345      350
Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
      355      360      365
Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
      370      375      380
Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385      390      395      400
Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
      405      410      415
Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
      420      425      430
Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
      435      440      445
Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
      450      455      460
Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465      470      475      480
His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
      485      490      495
Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
      500      505      510
Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
      515      520      525
Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
      530      535      540
Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545      550      555      560
Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
      565      570      575
Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
      580      585      590
Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
      595      600      605
Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
      610      615      620
Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625      630      635      640
Ala Trp Gly Gly Leu Glu His His His His His His
      645      650

```

<210> 819

<211> 132

<212> PRT

<213> Homo sapien

<400> 819

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
1      5      10      15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
      20      25      30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
      35      40      45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
      50      55      60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
65      70      75      80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala

```

305

	85		90		95										
Asp	Ala	Leu	Asn	Gly	His	His	Pro	Gly	Asp	Val	Ile	Ser	Val	Asn	Trp
	100			105									110		
Gln	Thr	Lys	Ser	Gly	Gly	Thr	Arg	Thr	Gly	Asn	Val	Thr	Leu	Ala	Glu
	115					120						125			
Gly	Pro	Pro	Ala												
	130														

<210> 820

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 820

ggggaattca tgatccggga gaaatttgcc cactgc

36

<210> 821

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 821

gggctcgagt caggagtttg agaccagcct ggc

33

<210> 822

<211> 675

<212> DNA

<213> Homo sapiens

<400> 822

atgcatcacc	atcaccatca	cacggccgcg	tccgataact	tccagctgtc	ccaggggtggg	60
cagggattcg	ccattccgat	cgggcaggcg	atggcgatcg	cgggccagat	caagcttccc	120
accgttcata	tcgggcctac	cgccttcctc	ggcttgggtg	ttgtcgacaa	caacggcaac	180
ggcgcacgag	tccaacgcgt	ggtcgggagc	gctccggcgg	caagtctcgg	catctccacc	240
ggcgacgtga	tcaccgcggt	cgacggcgct	ccgatcaact	cggccaccgc	gatggcggac	300
gcgcttaacg	ggcatcatcc	cggtgacgtc	atctcgggtg	cctggcaaac	caagtcgggc	360
ggcacgcgta	caggaacgt	gacattggcc	gagggacccc	cggccgaatt	catgatccgg	420
gagaaatttg	cccactgcac	cgtgctaacc	attgcacaca	gattgaacac	cattattgac	480
agcgacaaga	taatggtttt	agattcagga	agactgaaag	aatatgatga	gccgtatgtt	540
ttgctgcaaa	ataaagagag	cctattttac	aagatgggtg	aacaactggg	caaggcagaa	600
gccgctgccc	tcactgaaac	agcaaaacag	agatgggggt	tcaccatgtt	ggccaggctg	660
gtctcaaact	cctga					675

<210> 823

<211> 291

<212> DNA

<213> Homo sapiens

306

<400> 823

```

atgggggatcc gggagaaatt tgccactgc accgtgctaa ccattgcaca cagattgaac 60
accattattg acagcgacaa gataatggtt ttagattcag gaagactgaa agaatatgat 120
gagccgtatg ttttgctgca aaataaagag agcctatattt acaagatggt gcaacaactg 180
ggcaaggcag aagccgctgc cctcactgaa acagcaaaac agagatgggg tttcaccatg 240
ttggccaggc tgggtctcaaa ctccctcgag caccaccacc accaccactg a 291

```

<210> 824

<211> 1074

<212> DNA

<213> Homo sapiens

<400> 824

```

atgtcagcca ttgagagggt gtcagaggca atcgctcagca tccgaagaat ccagaccttt. 60
ttgctacttg atgagatatc acagcgcaac cgtcagctgc cgtcagatgg taaaagatg 120
gtgcatgtgc aggattttac tgctttttgg gataaggcat cagagacccc aactctacaa 180
ggcctttcct ttactgtcag acctggcgaa ttgttagctg tggtcggccc cgtgggagca 240
gggaagtcac cactgttaag tgccgtgctc ggggaattgg cccaagtca cgggctggtc 300
agcgtgcatg gaagaattgc ctatgtgtct cagcagccct ggggtgttctc ggggaactctg 360
aggagtaata ttttatttgg gaagaaatac gaaaaggaac gatatgaaa agtcataaag 420
gcttgtgctc tgaaaaagga tttacagctg ttggaggatg gtgatctgac tgtgatagga 480
gatcggggaa ccacgctgag tggagggcag aaagcacggg taaaccttgc aagagcagtg 540
tatcaagatg ctgacatcta tctcctggac gatcctctca gtgcagtaga tgcggaagtt 600
agcagacact tgttcgaact gtgtatttgt caaattttgc atgagaagat cacaatttta 660
gtgactcatc agttgcagta cctcaaagct gcaagtcaga ttctgatatt gaaagatggt 720
aaaatggtgc agaaggggac ttacactgag ttcctaaaat ctggtataga ttttggctcc 780
cttttaaaaga aggataatga ggaaagtga caacctccag ttccaggaac tcccacacta 840
aggaatcgta ccttctcaga gtcttcggtt tggctctcaac aatcttctag accctccttg 900
aaagatggtg ctctggagag ccaagataca gagaatgtcc cagttacact atcagaggag 960
aaccgttctg aaggaaaagt tggttttcag gcctataaga attacttcag agctggtgct 1020
cactggattg tcttcatttt ccttattctc gagcaccacc accaccacca ctga 1074

```

<210> 825

<211> 224

<212> PRT

<213> Homo sapiens

<400> 825

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5              10              15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20              25              30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35              40              45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50              55              60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65              70              75
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85              90              95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100             105             110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115             120             125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala
      130             135             140
His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp

```

307

```

145          150          155          160
Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp
          165          170          175
Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met
          180          185          190
Val Gln Gln Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala
          195          200          205
Lys Gln Arg Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
          210          215          220

```

<210> 826

<211> 357

<212> PRT

<213> Homo sapiens

<400> 826

```

Met Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg Arg
          5          10          15
Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg Gln
          20          25          30
Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala
          35          40          45
Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe
          50          55          60
Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly Ala
          65          70          75          80
Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro Ser
          85          90          95
His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln Gln
          100          105          110
Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly Lys
          115          120          125
Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala Leu
          130          135          140
Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile Gly
          145          150          155          160
Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn Leu
          165          170          175
Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp Pro
          180          185          190
Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu Cys
          195          200          205
Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His Gln
          210          215          220
Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp Gly
          225          230          235          240
Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly Ile
          245          250          255
Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln Pro
          260          265          270
Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu Ser
          275          280          285
Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly Ala
          290          295          300
Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu Glu
          305          310          315          320
Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr Phe

```

308

325 330 335
 Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Glu His
 340 345 350
 His His His His His
 355

<210> 827
 <211> 96
 <212> PRT
 <213> Homo sapiens

<400> 827
 Met Gly Ile Arg Glu Lys Phe Ala His Cys Thr Val Leu Thr Ile Ala
 5 10 15
 His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys Ile Met Val Leu Asp
 20 25 30
 Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr Val Leu Leu Gln Asn
 35 40 45
 Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln Leu Gly Lys Ala Glu
 50 55 60
 Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg Trp Gly Phe Thr Met
 65 70 75 80
 Leu Ala Arg Leu Val Ser Asn Ser Leu Glu His His His His His His
 85 90 95

<210> 828
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 828
 cgcccatggg gatccgggag aaatttgccc actgc 35

<210> 829
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 829
 cgccctgagg gagtttgaga ccagcctggc caaca 35

<210> 830
 <211> 38
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 830

309

gcatggacca tatgtcagcc attgagaggg tgtcagag 38

<210> 831
 <211> 34
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 831
 ccgctcgaga ataaggaaaa tgaagacaat ccag 34

<210> 832
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 832
 gttgaattca tgcacggggc ccagggtg 27

<210> 833
 <211> 30
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 833
 cccctcgagt cactatgggtc tgcctcttga 30

<210> 834
 <211> 915
 <212> DNA
 <213> Homo sapiens

<400> 834
 atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccaggggtggg 60
 cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
 accgttcata tcgggcctac cgccttcctc ggcttggtg ttgtcgacaa caacggcaac 180
 ggcgacagag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300
 ggccttaacg ggcacatcc cgggtgacgtc atctcgggtga cctggcaaac caagtcgggc 360
 ggacacgcgt cagggaacgt gacattggcc gagggacccc cggccgaatt catgcacggg 420
 ccccgagtg cggcacgctg ctccgagtg gettgtcctg ccttggtctg cacctctgcg 480
 ggggtgcgtc tggagggggt ggaccggcca ccaaccttac ccagtcaagg aagtggatgg 540
 ccatgttccc acagcctgag tggctgccac ctgatggctg atggagcaaa ggccttagga 600
 aaagcagatg gcccttggcc ctacctttt gttagaagaa ctgatgttc atgtcctgca 660
 gcgagtgagg ttggtggctg tgccccagc tcctggcgcg ccctcgaga ggtgactggt 720
 tgctctttgg gccctcttgg ccttgcccag catgcacaag cctcagtgct actactgtgc 780

310

tacaaatgga gccatatagg ggaaacgagc agccatctca ggagcaaggt gtatgctgcc 840
 ttgggggct ccagtccttg cctcaagggt cttatgtcac tgtgggcttc ttggttgta 900
 agaggcagac catag 915

<210> 835

<211> 304

<212> PRT

<213> Homo sapiens

<400> 835

Met	His	His	His	His	His	His	Thr	Ala	Ala	Ser	Asp	Asn	Phe	Gln	Leu
			5						10					15	
Ser	Gln	Gly	Gly	Gln	Gly	Phe	Ala	Ile	Pro	Ile	Gly	Gln	Ala	Met	Ala
		20					25					30			
Ile	Ala	Gly	Gln	Ile	Lys	Leu	Pro	Thr	Val	His	Ile	Gly	Pro	Thr	Ala
	35					40					45				
Phe	Leu	Gly	Leu	Gly	Val	Val	Asp	Asn	Asn	Gly	Asn	Gly	Ala	Arg	Val
	50					55				60					
Gln	Arg	Val	Val	Gly	Ser	Ala	Pro	Ala	Ala	Ser	Leu	Gly	Ile	Ser	Thr
65				70					75					80	
Gly	Asp	Val	Ile	Thr	Ala	Val	Asp	Gly	Ala	Pro	Ile	Asn	Ser	Ala	Thr
			85					90					95		
Ala	Met	Ala	Asp	Ala	Leu	Asn	Gly	His	His	Pro	Gly	Asp	Val	Ile	Ser
		100					105					110			
Val	Thr	Trp	Gln	Thr	Lys	Ser	Gly	Gly	Thr	Arg	Thr	Gly	Asn	Val	Thr
	115					120						125			
Leu	Ala	Glu	Gly	Pro	Pro	Ala	Glu	Phe	Met	His	Gly	Pro	Gln	Val	Leu
	130					135					140				
Ala	Arg	Cys	Ser	Glu	Cys	Ala	Cys	Pro	Ala	Leu	Ala	Ala	Thr	Ser	Ala
145				150					155					160	
Gly	Val	Arg	Leu	Glu	Gly	Val	Asp	Arg	Pro	Pro	Thr	Leu	Pro	Ser	Gln
			165					170					175		
Gly	Ser	Gly	Trp	Pro	Cys	Ser	His	Ser	Leu	Ser	Gly	Cys	His	Leu	Met
	180						185						190		
Ala	Asp	Gly	Ala	Lys	Ala	Leu	Gly	Lys	Ala	Asp	Gly	Pro	Trp	Pro	Tyr
	195					200					205				
Leu	Phe	Val	Arg	Arg	Thr	Asp	Val	Pro	Cys	Pro	Ala	Ala	Ser	Glu	Val
	210				215						220				
Gly	Gly	Cys	Ala	Pro	Ser	Trp	Arg	Ala	Leu	Ala	Glu	Val	Thr	Gly	
225				230					235					240	
Cys	Ser	Leu	Gly	Pro	Leu	Gly	Leu	Ala	Gln	His	Ala	Gln	Ala	Ser	Val
			245					250					255		
Leu	Leu	Leu	Cys	Tyr	Lys	Trp	Ser	His	Ile	Gly	Glu	Thr	Ser	Ser	His
	260						265						270		
Leu	Arg	Ser	Lys	Val	Tyr	Ala	Ala	Phe	Gly	Gly	Ser	Ser	Pro	Cys	Leu
	275					280					285				
Lys	Gly	Leu	Met	Ser	Leu	Trp	Ala	Ser	Trp	Leu	Ser	Arg	Gly	Arg	Pro
	290					295					300				

<210> 836

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 836

311

cgaagtcacg tggaggccag cctc

24

<210> 837

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 837

cctgaccgaa ttcattaact ggcctggac

29

<210> 838

<211> 166

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> (1)...(166)

<223> Xaa = Any Amino Acid

<400> 838

Met	Gly	His	His	His	His	His	His	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg
1				5					10					15	
His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile
			20					25					30		
Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser
		35					40					45			
Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly
	50					55				60					
Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val
65					70					75				80	
Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro
			85						90					95	
Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Xaa	Gln	Xaa
			100					105					110		
Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr
		115					120					125			
Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly
	130					135					140				
Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu
145					150					155					160
Lys	Thr	Val	Gln	Ala	Ser										
					165										

<210> 839

<211> 504

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(504)

<223> n = A,T,C or G

312

<400> 839
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 aacagaccct tgctcgctaa cgacctcatg ctcatcaagt tggacgaatc cgtgtccgag 120
 tctgacacca tccggagcat cagcattgct tcgcagtgcc ctaccgcggg gaactcttgc 180
 ctcgtttctg gctgggggtct gctggcgaaac ggcagaatgc ctaccgtgct gcagtgcgtg 240
 aacgtgtcgg tgggtgtctga ggaggtctgc agtaagctct atgaccgcgt gtaccacccc 300
 agcatgttct gcgccggcgg agggcaanac cagaangact cctgcaacgg tgactctggg 360
 gggcccctga tctgcaacgg gtacttgcag -ggccttgtgt ctttcggaaa agccccgtgt 420
 ggccaagttg gcgtgccagg tgtctacacc aacctctgca aattcactga gtggatagag 480
 aaaaccgtcc aggccagtta atga 504

<210> 840
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 840
 ctcagggttc cggagccgcg g 21

<210> 841
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 841
 ctatagaatt cattacaaa aagctgggct ccagc 35

<210> 842
 <211> 241
 <212> PRT
 <213> Homo sapiens

<400> 842
 Met Gln His His His His His Leu Arg Val Pro Glu Pro Arg Pro
 1 5 10 15
 Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro
 20 25 30
 Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg
 35 40 45
 Gln Gly Gly Arg Thr Ser Ser Gln Arg Gln Arg Asp Pro Glu Pro Glu
 50 55 60
 Pro Glu Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn
 65 70 75 80
 Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr
 85 90 95
 Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp
 100 105 110
 Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys
 115 120 125

313

Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile
 130 135 140
 Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu
 145 150 155 160
 Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys
 165 170 175
 Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser
 180 185 190
 Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys
 195 200 205
 Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn Ser Tyr
 210 215 220
 Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro Ala Phe
 225 230 235 240
 Trp

<210> 843
 <211> 729
 <212> DNA
 <213> Homo sapiens

<400> 843
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 gcggaggggg ccgcgcgcgc gaccccgctc aagccgctca cgtccttcct catccaggac 120
 atcctgcggg acggcgcgca gcggcaaggc ggccgcacga gcagccagag acagcgcgac 180
 ccggagccgg agccagagcc agagccagag ggaggacgca gccgcgccgg ggcgcagAAC 240
 gaccagctga gcaccggggc ccgcgcgcgc ccggatgagg ccgagacgct ggcagagacc 300
 gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgcctt 360
 ccaaggcttc cccaaacccc taagcagccg cagaagcgct cccgagctgc cttctccac 420
 actcaggtga tcgagttgga gaggaagttc agccatcaga agtacctgtc ggccccctgaa 480
 cgggccccacc tggccaagaa cctcaagctc acggagaccc aagtgaagat atggttccag 540
 aacagacgct ataagactaa gcgaaagcag ctctcctcgg agctgggaga cttggagaag 600
 cactcctttt tgccggccct gaaagaggag gccttctccc gggcctccct ggtctcctg 660
 tataacagct atccttacta cccatacctg cactgcgtgg gcagctggag cccagctttt 720
 tggtaatga 729

<210> 844
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 844
 ctactaagcg ctggagtgg ggtatcag 27

<210> 845
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

314

<400> 845
catcgagaat tcactactct ctgactagat gtc

33

<210> 846
<211> 161
<212> PRT
<213> Homo sapiens

<400> 846
Met Gln His His His His His Ala Gly Val Arg Asp Gln Gly Gln
1 5 10 15
Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly
20 25 30
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly
35 40 45
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys
50 55 60
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly
65 70 75 80
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val
85 90 95
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln
100 105 110
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro
115 120 125
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His
130 135 140
Gly Pro Pro Trp Leu Pro Asn Ala Leu Glu Arg Gly His Leu Val Arg
145 150 155 160
Glu

<210> 847
<211> 489
<212> DNA
<213> Homo sapiens

<400> 847
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cctcacacag ggaagagagg gcccctcctg cagggcctca cctgggccac aggaggacac 120
tgcttttctc ctgaggagtc aggagctgtg gatggtgctg gacagaagaa ggacagggcc 180
tggtctcaggt gtccagaggc tgcgctggc ttcccttttg gatcagactg cagggaggga 240
gggcggcagg gttgtggggg gagtgcgat gaggatgacc tgggggtggc tccaggcctt 300
gcccctgcct gggccctcac ccagcctccc tcacagtctc ctggccctca gtctctcccc 360
tccactccat cctccatctg gcctcagtgg gtcattctga tcaactgaact gaccataccc 420
agccctgccc acggccctcc atggctcccc aatgccctgg agaggggaca tctagtcaga 480
gagtagtga 489

<210> 848
<211> 132
<212> PRT
<213> Homo sapiens

<400> 848
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe

315

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      1             5             10             15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
      20             25             30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
      35             40             45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
      50             55             60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
      65             70             75             80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
      85             90             95
Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser Val Asn Trp
      100            105            110
Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr Leu Ala Glu
      115            120            125
Gly Pro Pro Ala
      130

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<210> 849

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 849

ggggaattca tcacctatgt gccgcctctg c

31

<210> 850

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 850

gggctcgagt cactcgccca cgaaatccgt gtaaaacagc

40

<210> 851

<211> 1203

<212> DNA

<213> Homo sapiens

<400> 851

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atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccaggggtggg 60
cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
accgttcata tcgggcctac cgccttcctc ggcttggtg ttgtcgacaa caacggcaac 180
ggcgacagag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300
gcgcttaacg ggcacatcc cggtgacgtc atctcgggtga cctggcaaac caagtccggc 360
ggcacgcgta caggaacgt gacattggcc gagggacccc cggccgaatt catcacctat 420
gtgccgcctc tgctgctgga agtgggggta gaggagaagt tcatgaccat ggtgctgggc 480
attggtccag tgctgggcct ggtctgtgtc ccgtcctag gctcagccag tgaccactgg 540
cgtggacgct atggccgccc cgggcccttc atctgggcac tgctcctggg catcctgctg 600

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316

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agcctctttc tcatcccaag ggccggctgg ctagcagggc tgctgtgccc ggatcccagg 660
cccctggagc tggcactgct catcctgggc gtggggctgc tggacttctg tggccagggtg 720
tgcttcactc cactggaggc cctgctctct gacctcttcc gggacccgga ccactgtcgc 780
caggcctact ctgtctatgc cttcatgata agtcttgggg gctgcctggg ctacctcctg 840
cctgccattg actgggacac cagtgccttg gccccctacc tgggcaccca ggaggagtgc 900
ctcttttgcc tgctcaccct catcttcctc acctgcgtag cagccacact gctggtggct 960
gaggaggcag cgctggggccc caccgagcca gcagaagggc tgtcggcccc ctccttgctg 1020
ccccactgct gtccatgccg ggcccgttg gctttccgga acctggggcgc cctgcttccc 1080
cggctgcacc agctgtgctg ccgcatgccc cgcacctgc gccggctctt cgtggtgag 1140
ctgtgcagct ggatggcact catgaccttc acgctgtttt acacggattt cgtgggcgag 1200
tga 1203

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<210> 852

<211> 400

<212> PRT

<213> Homo sapiens

<400> 852

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Met His His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5              10              15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20              25              30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35              40              45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50              55              60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65              70              75
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85              90              95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100             105             110
Val Thr Trp Gln Thr Lys Ser Gly Thr Arg Thr Gly Asn Val Thr
      115             120             125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Ile Thr Tyr Val Pro Pro Leu
      130             135             140
Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr Met Val Leu Gly
      145             150             155
Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
      165             170             175
Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
      180             185             190
Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
      195             200             205
Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
      210             215             220
Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val
      225             230             235
Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro
      245             250             255
Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
      260             265             270
Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser
      275             280             285
Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu
      290             295             300
Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala
      305             310             315             320

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317

Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala
 325 330 335
 Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe
 340 345 350
 Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys Cys Arg
 355 360 365
 Met Pro Arg Thr Leu Arg Arg Leu Phe Val Ala Glu Leu Cys Ser Trp
 370 375 380
 Met Ala Leu Met Thr Phe Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu
 385 390 395 400

<210> 853
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 853
 Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
 5 10 15
 Ser Val Arg Val
 20

<210> 854
 <211> 60
 <212> DNA
 <213> Homo sapiens

<400> 854
 ctgctccac ctccaccgc gctctgcggg gcctctgcct gtgatgtctc cgtacgtgtg 60

<210> 855
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 855
 Ala Ser Ala Cys Asp Val Ser Val Arg Val
 5 10

<210> 856
 <211> 30
 <212> DNA
 <213> Homo sapiens

<400> 856
 gcctctgcct gtgatgtctc cgtacgtgtg 30

<210> 857
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 857
 Ala Ser Ala Cys Asp Val Ser Val Arg
 1 5

<210> 858

318

<211> 9
<212> PRT
<213> Homo sapiens

<400> 858
Ser Ala Cys Asp Val Ser Val Arg Val
5

<210> 859
<211> 27
<212> DNA
<213> Homo sapiens

<400> 859
tctgcctgtg atgtctecgt acgtgtg

27

<210> 860
<211> 19
<212> PRT
<213> Homo sapiens

<400> 860
Gly Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser
5 10 15
Ala Ser Asp

<210> 861
<211> 19
<212> PRT
<213> Homo sapiens

<400> 861
Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr
5 10 15
Met Val Leu

<210> 862
<211> 19
<212> PRT
<213> Homo sapiens

<400> 862
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
5 10 15
Gln Leu Leu

<210> 863
<211> 57
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(57)
<223> n = A,T,C or G

319

<400> 863
ggathggnc cngtntngg nytngtntgy gtnccnytny tnggnwsngc nwsngay 57

<210> 864
<211> 57
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(57)
<223> n = A,T,C or G

<400> 864
gtncnccny tnytnytnga rgtnggngtn gargaraart tyatgacnat ggtnytn 57

<210> 865
<211> 57
<212> DNA
<213> Homo sapiens

<220>
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<222> (1)...(57)
<223> n = A,T,C or G

<400> 865
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<210> 866
<211> 9
<212> PRT
<213> Homo sapiens

<400> 866
Val Leu Gln Cys Val Asn Val Ser Val
1 5

<210> 867
<211> 9
<212> PRT
<213> Homo sapiens

<400> 867
Arg Met Pro Thr Val Leu Gln Cys Val
1 5

<210> 868
<211> 9
<212> PRT
<213> Homo sapiens

<400> 868
Asn Leu Cys Lys Phe Thr Glu Trp Ile
1 5

320

<210> 869
<211> 9
<212> PRT
<213> Homo sapiens

<400> 869
Met Leu Ile Lys Leu Asp Glu Ser Val
1 5

<210> 870
<211> 9
<212> PRT
<213> Homo sapiens

<400> 870
Leu Leu Ala Asn Asp Leu Met Leu Ile
1 5

<210> 871
<211> 10
<212> PRT
<213> Homo sapiens

<400> 871
Leu Leu Ala Asn Gly Arg Met Pro Thr Val
1 5 10

<210> 872
<211> 10
<212> PRT
<213> Homo sapiens

<400> 872
Leu Met Leu Ile Lys Leu Asp Glu Ser Val
1 5 10

<210> 873
<211> 10
<212> PRT
<213> Homo sapiens

<400> 873
Val Leu Gln Cys Val Asn Val Ser Val Val
1 5 10

<210> 874
<211> 10
<212> PRT
<213> Homo sapiens

<400> 874
Gly Leu Leu Ala Asn Gly Arg Met Pro Thr
1 5 10

<210> 875
<211> 10
<212> PRT

321

<213> Homo sapiens

<400> 875

Thr Val Leu Gln Cys Val Asn Val Ser Val
1 5 10

<210> 876

<211> 9

<212> PRT

<213> Homo sapiens

<400> 876

Gly Val Leu Val His Pro Gln Trp Val
1 5

<210> 877

<211> 9

<212> PRT

<213> Homo sapiens

<400> 877

Val Leu Val His Pro Gln Trp Val Leu
1 5

<210> 878

<211> 1195

<212> DNA

<213> Homo sapiens

<400> 878

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ggagaaatgt agaagaagac gattatttgc ataaggacac gggagagacc agcatgctaa 180
aaagacctgt gcttttgcac ttgcaccaa cagcccatgc tgatgaattt gactgccctt 240
cagaacttca gcacacacag gaactcttcc cacagtggca cttgcccaatt aaaatagctg 300
ctattatagc atctctgact tttctttaca ctctctgag ggaagtaatt caccctttag 360
caacttccca tcaacaatat ttttataaaa ttccaatcct ggcatcaaac aaagtcttgc 420
caatggtttc catcactctc ttggcattgg tttacctgcc aggtgtgata gcagcaattg 480
tccaacttca taatggaacc aagtataaga agtttcaca ttggttggat aagtggatgt 540
taacaagaaa gcagtttggg cttctcagtt tcttttttgc tgtactgcat gcaatttata 600
gtctgtctta cccaatgagg cgatcctaca gatacaagtt gctaaaactgg gcataatcaac 660
aggtccaaca aaataaagaa gatgcctgga ttgagcatga tgtttggaga atggagattt 720
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agattagaca tggttgggaa gacgtcacca aaattaacaa aactgagata tgttccagat 1080
tgtagaatta ctgtttacac acatttttgt tcaatattga tatattttat caccaacatt 1140
tcaagtttgt atttgttaat aaaatgatta ttcaaggaaa aaaaaaaaaa aaaaa 1195

<210> 879

<211> 339

<212> PRT

<213> Homo sapiens

322

<400> 879

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
      5              10              15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20              25              30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35              40              45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50              55              60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65              70              75              80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85              90              95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100             105             110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115             120             125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130             135             140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145             150             155             160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165             170             175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180             185             190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195             200             205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210             215             220
Val Gly Leu Ala Ile Leu Ala Leu Ala Val Thr Ser Ile Pro Ser
      225             230             235             240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
      245             250             255
Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
      260             265             270
Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
      275             280             285
Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
      290             295             300
Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
      305             310             315             320
Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
      325             330             335
Ser Gln Leu

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<210> 880

<211> 2172

<212> DNA

<213> Homo sapiens

<400> 880

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aaaattgaat attgagatac cattctttag tgttaccttt tttacccaca tgtgtttctg 60
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ccatttttagt actatgggtg agtacatgga attgaagtct ggcttaaatc ttcagaaagt 180
tatatatcta ttttatttta tttttttgag acagagtctc gctgtgtcac ccaggctgga 240
gtgcggtgcc acaatcttgg ctcaactgcaa cctctgagtc ccaggttcaa gcgatactca 300
tgcctcggcc tcctgagtag ctgggactac aggcgtgcac caccacatct ggctaattctt 360
tttttgtatt tttagtagag acgggggtttc actgtggtct ccatctcctg acctcgtgat 420

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ccgcctgcct cccaaagtgc tgggattaca ggcatgagcc accgcacaca gctgggactg 480
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aggaaactta caatcatggt ggaaggcgaa ggggaagcaa ggcacgtctt acatgggtggc 600
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<210> 881

<211> 2455

<212> DNA

<213> Homo sapiens

<400> 881

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```

<210> 882

<211> 2455

<212> DNA

<213> Homo sapiens

<400> 882

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325

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```

<210> 883

<211> 62

<212> PRT

<213> Homo sapiens

<400> 883

```

Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
                    5                      10                      15
His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
                    20                      25                      30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
                    35                      40                      45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
                    50                      55                      60

```

<210> 884

<211> 135

<212> PRT

<213> Homo sapiens

<400> 884

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
                    5                      10                      15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
                    20                      25                      30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
                    35                      40                      45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
                    50                      55                      60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
                    65                      70                      75                      80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
                    85                      90                      95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
                    100                     105                     110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
                    115                     120                     125
Leu Leu Asn Tyr Gln Val Ser
                    130                     135

```

<210> 885

<211> 77

<212> PRT

<213> Homo sapiens

<400> 885

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln

```

326

```

          5          10          15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
          20          25          30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
          35          40          45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
          50          55          60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
          65          70          75

```

<210> 886

<211> 60

<212> PRT

<213> Homo sapiens

<400> 886

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

<210> 887

<211> 76

<212> PRT

<213> Homo sapiens

<400> 887

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

<210> 888

<211> 76

<212> PRT

<213> Homo sapiens

<400> 888

```

Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
          5          10          15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
          20          25          30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
          35          40          45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
          50          55          60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
          65          70          75

```

327

<210> 889
 <211> 80
 <212> PRT
 <213> Homo sapiens

<400> 889
 Met Leu Leu His Ser Ser Leu Val Asn Arg Ala Arg Leu Cys Leu Lys
 5 10 15
 Asn Lys Gln Ile Asn Lys Gln Thr Asn Lys Thr Glu Arg Phe Cys Cys
 20 25 30
 Asn Val Gln Gly Ala Ile Cys Ser Phe Lys Lys Ile Ile Phe Gly Gln
 35 40 45
 Ala Gln Trp Leu Thr Pro Val Ile Pro Ala Leu Trp Glu Ala Lys Val
 50 55 60
 Gly Gly Ser Phe Glu Val Arg Ser Leu Arg Ser Ala Trp Pro Thr Trp
 65 70 75 80

<210> 890
 <211> 72
 <212> PRT
 <213> Homo sapiens

<400> 890
 Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro His Asn Pro
 5 10 15
 Ile Thr Ser His Gln Val Ser Ser Asp Thr Trp Asp Trp Val Gly Thr
 20 25 30
 Gln Ser Gln Thr Val Ser Asp Ala Ala Gly Ala Gly Asp Thr Glu Thr
 35 40 45
 Thr Gln Thr Trp Cys Leu Cys His Ser Ser Gly Leu Cys Leu Ser Pro
 50 55 60
 Gly Pro Pro Ser Pro Ser Met Val
 65 70

<210> 891
 <211> 77
 <212> PRT
 <213> Homo sapiens

<400> 891
 Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln
 5 10 15
 Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
 20 25 30
 Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
 35 40 45
 Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
 50 55 60
 Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
 65 70 75

<210> 892
 <211> 60
 <212> PRT
 <213> Homo sapiens

<400> 892

328

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
                    5              10              15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
                    20              25              30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
                    35              40              45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
                    50              55              60

```

<210> 893

<211> 76

<212> PRT

<213> Homo sapiens

<400> 893

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
                    5              10              15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
                    20              25              30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
                    35              40              45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
                    50              55              60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
                    65              70              75

```

<210> 894

<211> 2479

<212> DNA

<213> Homo sapiens

<400> 894

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cggaaaaccc ctatcccgca cagccactg tggccccac tgtctacgag gtgcatccgg 180
ctcagtacta cccgtccccc gtgccccagt acgccccgag ggtcctgacg caggcttcca 240
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329

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<210> 895

<211> 492

<212> PRT

<213> Homo sapiens

<400> 895

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Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20              25              30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35              40              45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50              55              60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65              70              75              80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85              90              95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100             105             110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115             120             125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130             135             140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145             150             155             160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165             170             175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180             185             190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195             200             205
Phe Met Lys Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys
      210             215             220
Leu Tyr His Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg
      225             230             235             240
Cys Leu Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
      245             250             255
Val Gly Gly Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser
      260             265             270
Leu His Val Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro

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		275						280					285			
Glu	Trp	Ile	Val	Thr	Ala	Ala	His	Cys	Val	Glu	Lys	Pro	Leu	Asn	Asn	
	290					295					300					
Pro	Trp	His	Trp	Thr	Ala	Phe	Ala	Gly	Ile	Leu	Arg	Gln	Ser	Phe	Met	
305					310					315					320	
Phe	Tyr	Gly	Ala	Gly	Tyr	Gln	Val	Gln	Lys	Val	Ile	Ser	His	Pro	Asn	
				325					330					335		
Tyr	Asp	Ser	Lys	Thr	Lys	Asn	Asn	Asp	Ile	Ala	Leu	Met	Lys	Leu	Gln	
			340					345					350			
Lys	Pro	Leu	Thr	Phe	Asn	Asp	Leu	Val	Lys	Pro	Val	Cys	Leu	Pro	Asn	
		355					360					365				
Pro	Gly	Met	Met	Leu	Gln	Pro	Glu	Gln	Leu	Cys	Trp	Ile	Ser	Gly	Trp	
	370					375					380					
Gly	Ala	Thr	Glu	Glu	Lys	Gly	Lys	Thr	Ser	Glu	Val	Leu	Asn	Ala	Ala	
385					390					395					400	
Lys	Val	Leu	Leu	Ile	Glu	Thr	Gln	Arg	Cys	Asn	Ser	Arg	Tyr	Val	Tyr	
				405					410					415		
Asp	Asn	Leu	Ile	Thr	Pro	Ala	Met	Ile	Cys	Ala	Gly	Phe	Leu	Gln	Gly	
			420					425				430				
Asn	Val	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Thr	Ser	
		435					440				445					
Asn	Asn	Asn	Ile	Trp	Trp	Leu	Ile	Gly	Asp	Thr	Ser	Trp	Gly	Ser	Gly	
	450					455					460					
Cys	Ala	Lys	Ala	Tyr	Arg	Pro	Gly	Val	Tyr	Gly	Asn	Val	Met	Val	Phe	
465					470					475					480	
Thr	Asp	Trp	Ile	Tyr	Arg	Gln	Met	Lys	Ala	Asn	Gly					
				485					490							

<400> 896							
gtcatattga	acattccaga	tacctatcat	tactcgatgc	tgttgataac	agcaagatgg	60	
ctttgaactc	agggtcacca	ccagctattg	gaccttacta	tgaaaaccat	ggataccaac	120	
cggaaaacc	ctatcccgcg	cagcccactg	tggtcccacg	tgctctacgag	gtgcctccgg	180	
ctcagtaata	cccgctcccc	gtgcccagtg	acgccccgag	ggctctcagc	caggcttcca	240	
accccgtcgt	ctgcacgcag	cccaaatccc	catccgggac	agtgtgcacc	tcaaagacta	300	
agaaagcact	gtgcatcacc	ttgacctctg	ggaccttcct	cgtgggagct	gcgctggccg	360	
ctggcctact	ctggaagttc	atgggcagca	agtgtctcaa	ctctgggata	gagtggcact	420	
cctcaggtac	ctgcataaac	ccctctaact	ggtgtgatgg	cgtgtcacac	tgccccggcg	480	
gggaggacga	gaatcggtgt	gttcgcctct	acggaccaa	cttcacctt	cagatgtact	540	
catctcagag	gaagtcctg	caccctgtgt	gccaagacga	ctggaacgag	aactacgggc	600	
gggggcctg	cagggacatg	ggctataaga	ataattttta	ctctagccaa	ggaatagtgg	660	
atgacagcgg	atccaccagc	ttt				683	

<400> 897
Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
1 5 10 15

331

Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
 20 25 30
 Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
 35 40 45
 Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
 50 55 60
 Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
 65 70 75 80
 Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
 85 90 95
 Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
 100 105 110
 Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
 115 120 125
 Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
 130 135 140
 Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
 145 150 155 160
 Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
 165 170 175
 Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
 180 185 190
 Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
 195 200 205
 Phe

<210> 898
 <211> 27
 <212> PRT
 <213> Homo sapiens

<400> 898
 Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
 1 5 10 15
 Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg
 20 25

<210> 899
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 899
 ggatccgccg ccaccatgtc actttctagc ctgct

35

<210> 900
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 900

332

gtcgactcag ctggaccaca gccgcag

27

<210> 901

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 901

ggatccgccg ccacatggg ctgcaggctg ctct

34

<210> 902

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 902

gtcgactcag aaatcctttc tcttgac

27

<210> 903

<211> 936

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...()

<223> n = A,T,C or G

<400> 903

atgggctgca ggctgntctg ctgtgcggtt ctctgtctcc tgggagcggg ccccatggaa 60
acgggagtta cgcagacacc aagacacctg gtcattggaa tgacaaataa gaagtctttg 120
aaatgtgaac aacatctggg tcataacgct atgtattggg acaagcaaag tgctaagaag 180
ccactggagc tcatgtttgt ctacagtctt gaagaacggg ttgaaaacaa cagtgtgcc 240
agtcgcttct cacctgaatg ccccaacagc tctcaottat tccttcacct acacacctg 300
cagccagaag actcggccct gtatctctgc gccagcagcc aagaccggac aagcagctcc 360
tacgagcagt acttcggggc gggcaccagg ctacaggtca cagaggacct gaaaaacgtg 420
ttcccaccgg aggtcgctgt gtttgagcca tcagaagcag agatctccca caccctaaag 480
gccacactgg tgtgcctggc cacaggcttc taccocgacc acgtggagct gagctgggtg 540
gtgaatggga aggaggtgca cagtggggtc agcacagacc cgcagccct caaggagcag 600
ccgcccctca atgactccag atactgcctg agcagccgcc tgagggtctc ggccaccttc 660
tggcagaacc cccgcaacca cttccgctgt caagtccagt tctacgggct ctcggagaat 720
gacgagtgga cccaggatag ggccaaacct gtcaccaga tcgtcagcgc cgaggccttg 780
ggtagagcag actgtggctt cacctccgag tcttaccagc aaggggtcct gtctgccacc 840
atcctctatg agatcttgct agggaaggcc accttgatg ccgtgctggg cagtgccttc 900
gtgctgatgg ccatgggtcaa gagaaaggat ttctga 936

<210> 904

<211> 834

<212> DNA

<213> Homo sapiens

333

<220>

<221> misc_feature

<222> (1)...()

<223> n = A,T,C or G

<400> 904

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atgtcacttt ctagcctgct naaggtggtc acagcttcac tgtggctagg acctggcatt 60
gccagaaga taactcaaac ccaaccagga atgttcgtgc aggaaaagga ggctgtgact 120
ctggactgca catatgacac cagtgatcaa agttatggtc tcttctggta caagcagccc 180
agcagtgggg aaatgatttt tcttatttat caggggtctt atgacgagca aaatgcaaca 240
gaaggtcgct actcattgaa ttccagaag gcaagaaaat ccgccaacct tgatcatctcc 300
gcttcacaac tgggggactc agcaatgtat ttctgtgcaa tgagagaggg cgcgggagga 360
ggaaacaaac tcacctttgg gacaggcact cagctaaaag tggaactcaa tatccagaac 420
cctgaccctg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgccta 480
ttcaccgatt ttgattctca aacaaatgtg tcacaaagta aggattctga tgtgtatatc 540
acagacaaaa ctgtgctaga catgaggtct atggacttca agagcaacag tgctgtggcc 600
tgagagcaaca aatctgactt tgcattgtgca aacgccttca acaacagcat tattccagaa 660
gacaccttct tcccagcccc agaaagttcc tgtgatgtca agctgggtcga gaaaagcttt 720
gaaacagata cgaacctaaa ctttcaaaac ctgtcagtga ttgggttccg acctctctc 780
ctgaaagtgg ccgggtttaa tctgctcatg acgctgcggc tgtggtccag ctga 834

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<210> 905

<211> 311

<212> PRT

<213> Homo sapiens

<220>

<221> variant

<222> (1)...(311)

<223> Xaa = Any amino acid

<400> 905

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Met Gly Cys Arg Leu Xaa Cys Cys Ala Val Leu Cys Leu Leu Gly Ala
      5              10              15
Val Pro Met Glu Thr Gly Val Thr Gln Thr Pro Arg His Leu Val Met
      20              25              30
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Leu Gly His
      35              40              45
Asn Ala Met Tyr Trp Tyr Lys Gln Ser Ala Lys Lys Pro Leu Glu Leu
      50              55              60
Met Phe Val Tyr Ser Leu Glu Glu Arg Val Glu Asn Asn Ser Val Pro
      65              70              75              80
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser His Leu Phe Leu His
      85              90              95
Leu His Thr Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser
      100             105             110
Ser Gln Asp Arg Thr Ser Ser Ser Tyr Glu Gln Tyr Phe Gly Pro Gly
      115             120             125
Thr Arg Leu Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu
      130             135             140
Val Ala Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys
      145             150             155             160
Ala Thr Leu Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu
      165             170             175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr
      180             185             190
Asp Pro Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr
      195             200             205

```

334

Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro
 210 215 220
 Arg Asn His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn
 225 230 235 240
 Asp Glu Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser
 245 250 255
 Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr
 260 265 270
 Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly
 275 280 285
 Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala
 290 295 300
 Met Val Lys Arg Lys Asp Phe
 305 310

<210> 906
 <211> 277
 <212> PRT
 <213> Homo sapiens

<400> 906
 Met Ser Leu Ser Ser Leu Leu Lys Val Val Thr Ala Ser Leu Trp Leu
 5 10 15
 Gly Pro Gly Ile Ala Gln Lys Ile Thr Gln Thr Gln Pro Gly Met Phe
 20 25 30
 Val Gln Glu Lys Glu Ala Val Thr Leu Asp Cys Thr Tyr Asp Thr Ser
 35 40 45
 Asp Gln Ser Tyr Gly Leu Phe Trp Tyr Lys Gln Pro Ser Ser Gly Glu
 50 55 60
 Met Ile Phe Leu Ile Tyr Gln Gly Ser Tyr Asp Glu Gln Asn Ala Thr
 65 70 75 80
 Glu Gly Arg Tyr Ser Leu Asn Phe Gln Lys Ala Arg Lys Ser Ala Asn
 85 90 95
 Leu Val Ile Ser Ala Ser Gln Leu Gly Asp Ser Ala Met Tyr Phe Cys
 100 105 110
 Ala Met Arg Glu Gly Ala Gly Gly Gly Asn Lys Leu Thr Phe Gly Thr
 115 120 125
 Gly Thr Gln Leu Lys Val Glu Leu Asn Ile Gln Asn Pro Asp Pro Ala
 130 135 140
 Val Tyr Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu
 145 150 155 160
 Phe Thr Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser
 165 170 175
 Asp Val Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp
 180 185 190
 Phe Lys Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala
 195 200 205
 Cys Ala Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe
 210 215 220
 Pro Ser Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe
 225 230 235 240
 Glu Thr Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe
 245 250 255
 Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu
 260 265 270
 Arg Leu Trp Ser Ser
 275

335

<210> 907
 <211> 1536
 <212> DNA
 <213> Homo sapiens

<400> 907
 atgtacaacc tgttgctgtc ctacgacaga catggggacc acctgcagcc cctggacctc 60
 gtgccaatc accaggtct caccctttc aagctggctg gaggaggagg taacactgtg 120
 atgtttcagc acctgatgca gaagcggaag cacaccagtg ggacgtatgg accactgacc 180
 tcgactctct atgacctcac agagatcgac toctcagggg atgagcagtc cctgctggaa 240
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300
 gagctggtga gcctcaagtga gaagcgggtac gggcgccgt acttctgcat gctgggtgcc 360
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgccc cctcaagccc 420
 aggaccaata accgcacgag ccccgaggac aacacctct tacagcagaa gctacttcag 480
 gaagcctaca tgaccctaa ggacgatatc cggctggtcg gggagctggt gactgtcatt 540
 ggggctatca tcatcctgct ggtagagggt ccagacatct tcagaatggg ggtcactcgc 600
 ttctttggag agaccatcct tgggggcccc ttccatgtcc tcatcatcac ctatgccttc 660
 atggtgctgg tgaccatggt gatgcggctc atcagtgccg gcggggagggt ggtaccatg 720
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagggt attccagatg 780
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900
 gaggaccccg aggagctagg ccacttctac gactacccca tggccctgtt cagcaccttc 960
 gagctgttcc ttaccatcat cgatggccca gccaaactaca acgtggacct gcccttcatt 1020
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080
 attgccatga tgggcgacac tcaactggcg gtggcccatg agcgggatga gctgtggagg 1140
 gccagattg tggccaccac ggtgatgctg gagcggaagc tgccctcgctg cctgtggcct 1200
 cgctccggga tctgcggacg ggagtatggc ctggggagacc gctgggtcct gcgggtggaa 1260
 gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacaccggg 1320
 ggctctgagg atttgacaa agactcagtg gaaaaactag agctgggctg tcccttcagc 1380
 cccacactgt cccttcctat gccctcagtg tctcgaagta cctcccgag cagtggcaat 1440
 tgggaaggc ttcggcaagg gaccctgagg agagacctgc gtgggataat caacagggggt 1500
 ctggaggacg gggagagctg ggaatatcag atctga 1536

<210> 908
 <211> 1533
 <212> DNA
 <213> Homo sapiens

<400> 908
 atgtacaacc tgttgctgtc ctacgacaga catggggacc acctgcagcc cctggacctc 60
 gtgccaatc accaggtct caccctttc aagctggctg gaggaggagg taacactgtg 120
 atgtttcagc acctgatgca gaagcggaag cacaccagtg ggacgtatgg accactgacc 180
 tcgactctct atgacctcac agagatcgac toctcagggg atgagcagtc cctgctggaa 240
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300
 gagctggtga gcctcaagtga gaagcgggtac gggcgccgt acttctgcat gctgggtgcc 360
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgccc cctcaagccc 420
 aggaccaata accgcacgag ccccgaggac aacacctct tacagcagaa gctacttcag 480
 gaagcctaca tgaccctaa ggacgatatc cggctggtcg gggagctggt gactgtcatt 540
 ggggctatca tcatcctgct ggtagagggt ccagacatct tcagaatggg ggtcactcgc 600
 ttctttggag agaccatcct tgggggcccc ttccatgtcc tcatcatcac ctatgccttc 660
 atggtgctgg tgaccatggt gatgcggctc atcagtgccg gcggggagggt ggtaccatg 720
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagggt attccagatg 780
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900
 gaggaccccg aggagctagg ccacttctac gactacccca tggccctgtt cagcaccttc 960
 gagctgttcc ttaccatcat cgatggccca gccaaactaca acgtggacct gcccttcatt 1020
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080

336

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attgccatga tgggcgacac tcactggcga gtggcccatg agcgggatga gctgtggagg 1140
gccagattg tggccaccac ggtgatgctg gagcggaagc tgcctcgctg cctgtggcct 1200
cgctccggga tctgcggacg ggagtatggc ctgggagacc gctggttcct gcgggtggaa 1260
gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacaccg 1320
ggctctgagg atttggacaa agactcagtg gaaaaactag agctgggctg tcccttcagc 1380
ccccacctgt cccttcctat gccctcagtg tctcgaagta cctcccgag cagtccaat 1440
tgggaaagc ttcggcaagg gaccctgagg agagacctgc gtgggataat caacaggggt 1500
ctggaggacg gggagagctg ggaatatcag atc 1533

```

<210> 909

<211> 511

<212> PRT

<213> Homo sapiens

<400> 909

```

Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
      5                               10                               15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
      20                               25                               30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
      35                               40                               45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
      50                               55                               60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
      65                               70                               75                               80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
      85                               90                               95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
      100                              105                              110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
      115                              120                              125
Phe Thr Met Cys Cys Ile Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn
      130                              135                              140
Arg Thr Ser Pro Arg Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln
      145                              150                              155                              160
Glu Ala Tyr Met Thr Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu
      165                              170                              175
Val Thr Val Ile Gly Ala Ile Ile Ile Leu Leu Val Glu Val Pro Asp
      180                              185                              190
Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln Thr Ile Leu Gly
      195                              200                              205
Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe Met Val Leu Val
      210                              215                              220
Thr Met Val Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met
      225                              230                              235                              240
Ser Phe Ala Leu Val Leu Gly Trp Cys Asn Val Met Tyr Phe Ala Arg
      245                              250                              255
Gly Phe Gln Met Leu Gly Pro Phe Thr Ile Met Ile Gln Lys Met Ile
      260                              265                              270
Phe Gly Asp Leu Met Arg Phe Cys Trp Leu Met Ala Val Val Ile Leu
      275                              280                              285
Gly Phe Ala Ser Ala Phe Tyr Ile Ile Phe Gln Thr Glu Asp Pro Glu
      290                              295                              300
Glu Leu Gly His Phe Tyr Asp Tyr Pro Met Ala Leu Phe Ser Thr Phe
      305                              310                              315                              320
Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro Ala Asn Tyr Asn Val Asp
      325                              330                              335
Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala Ala Phe Ala Ile Ile Ala

```

337

```

          340          345          350
Thr Leu Leu Met Leu Asn Leu Leu Ile Ala Met Met Gly Asp Thr His
          355          360          365
Trp Arg Val Ala His Glu Arg Asp Glu Leu Trp Arg Ala Gln Ile Val
          370          375          380
Ala Thr Thr Val Met Leu Glu Arg Lys Leu Pro Arg Cys Leu Trp Pro
385          390          395          400
Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly Leu Gly Asp Arg Trp Phe
          405          410          415
Leu Arg Val Glu Asp Arg Gln Asp Leu Asn Arg Gln Arg Ile Gln Arg
          420          425          430
Tyr Ala Gln Ala Phe His Thr Arg Gly Ser Glu Asp Leu Asp Lys Asp
          435          440          445
Ser Val Glu Lys Leu Glu Leu Gly Cys Pro Phe Ser Pro His Leu Ser
          450          455          460
Leu Pro Met Pro Ser Val Ser Arg Ser Thr Ser Arg Ser Ser Ala Asn
465          470          475          480
Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg Arg Asp Leu Arg Gly Ile
          485          490          495
Ile Asn Arg Gly Leu Glu Asp Gly Glu Ser Trp Glu Tyr Gln Ile
          500          505          510

```

<210> 910

<211> 134

<212> PRT

<213> Homo sapiens

<400> 910

```

Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
          5          10          15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
          20          25          30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
          35          40          45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
          50          55          60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
          65          70          75          80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
          85          90          95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
          100          105          110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
          115          120          125
Phe Thr Met Cys Cys Ile
          130

```

<210> 911

<211> 55

<212> PRT

<213> Homo sapiens

<400> 911

```

Ala Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn Arg Thr Ser Pro Arg
          5          10          15
Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln Glu Ala Tyr Met Thr
          20          25          30
Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu Val Thr Val Ile Gly

```

338

35 40 45
 Ala Ile Ile Ile Leu Leu Val
 50 55

<210> 912
 <211> 39
 <212> PRT
 <213> Homo sapiens

<400> 912
 Glu Val Pro Asp Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln
 5 10 15
 Thr Ile Leu Gly Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe
 20 25 30
 Met Val Leu Val Thr Met Val
 35

<210> 913
 <211> 19
 <212> PRT
 <213> Homo sapiens

<400> 913
 Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met Ser Phe Ala
 5 10 15
 Leu Val Leu

<210> 914
 <211> 52
 <212> PRT
 <213> Homo sapiens

<400> 914
 Gly Trp Cys Asn Val Met Tyr Phe Ala Arg Gly Phe Gln Met Leu Gly
 5 10 15
 Pro Phe Thr Ile Met Ile Gln Lys Met Ile Phe Gly Asp Leu Met Arg
 20 25 30
 Phe Cys Trp Leu Met Ala Val Val Ile Leu Gly Phe Ala Ser Ala Phe
 35 40 45
 Tyr Ile Ile Phe
 50

<210> 915
 <211> 213
 <212> PRT
 <213> Homo sapiens

<400> 915
 Gln Thr Glu Asp Pro Glu Glu Leu Gly His Phe Tyr Asp Tyr Pro Met
 5 10 15
 Ala Leu Phe Ser Thr Phe Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro
 20 25 30
 Ala Asn Tyr Asn Val Asp Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala
 35 40 45
 Ala Phe Ala Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Leu Ile Ala
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 Met Met Gly Asp Thr His Trp Arg Val Ala His Glu Arg Asp Glu Leu

339

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65          70          75          80
Trp Arg Ala Gln Ile Val Ala Thr Thr Val Met Leu Glu Arg Lys Leu
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Pro Arg Cys Leu Trp Pro Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly
          100          105          110
Leu Gly Asp Arg Trp Phe Leu Arg Val Glu Asp Arg Gln Asp Leu Asn
          115          120          125
Arg Gln Arg Ile Gln Arg Tyr Ala Gln Ala Phe His Thr Arg Gly Ser
          130          135          140
Glu Asp Leu Asp Lys Asp Ser Val Glu Lys Leu Glu Leu Gly Cys Pro
          145          150          155          160
Phe Ser Pro His Leu Ser Leu Pro Met Pro Ser Val Ser Arg Ser Thr
          165          170          175
Ser Arg Ser Ser Ala Asn Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg
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<210> 916

<211> 1302

<212> DNA

<213> Homo sapiens

<400> 916

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<210> 917

<211> 2061

<212> DNA

<213> Homo sapiens

<400> 917

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340

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<210> 918

<211> 957

<212> DNA

<213> Homo sapiens

<400> 918

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<210> 919

341

<211> 954

<212> DNA

<213> Homo sapiens

<400> 919

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<211> 318

<212> PRT

<213> Homo sapiens

<400> 920

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          20          25          30
Pro Leu Cys Ser Leu Tyr Leu Ile Ala Val Leu Gly Asn Leu Thr Ile
          35          40          45
Ile Tyr Ile Val Arg Thr Glu His Ser Leu His Glu Pro Met Tyr Ile
          50          55          60
Phe Leu Cys Met Leu Ser Gly Ile Asp Ile Leu Ile Ser Thr Ser Ser
          65          70          75          80
Met Pro Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln
          85          90          95
Phe Asp Ala Cys Leu Leu Gln Met Phe Ala Ile His Ser Leu Ser Gly
          100          105          110
Met Glu Ser Thr Val Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala
          115          120          125
Ile Cys His Pro Leu Arg His Ala Thr Val Leu Thr Leu Pro Arg Val
          130          135          140
Thr Lys Ile Gly Val Ala Ala Val Val Arg Gly Ala Ala Leu Met Ala
          145          150          155          160
Pro Leu Pro Val Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile
          165          170          175
Leu Ser His Ser Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys
          180          185          190
Asp Asp Ile Arg Val Asn Val Val Tyr Gly Leu Ile Val Ile Ile Ser
          195          200          205
Ala Ile Gly Leu Asp Ser Leu Leu Ile Ser Phe Ser Tyr Leu Leu Ile
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342

Gly Thr Cys Val Ser His Val Cys Ala Val Phe Ile Phe Tyr Val Pro
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 260 265 270
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<210> 921
 <211> 28
 <212> PRT
 <213> Homo sapiens

<400> 921
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 <212> PRT
 <213> Homo sapiens

<400> 922
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<210> 923
 <211> 21
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<400> 923
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 Ala Cys Leu Leu Gln
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<210> 924
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 <213> Homo sapiens

<400> 924
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<210> 925
 <211> 37
 <212> PRT
 <213> Homo sapiens

343

<400> 925

Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile Leu Ser His Ser
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 Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys Asp Asp Ile Arg
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 Val Asn Val Val Tyr
 35

<210> 926

<211> 13

<212> PRT

<213> Homo sapiens

<400> 926

Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys
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<210> 927

<211> 10

<212> PRT

<213> Homo sapiens

<400> 927

Val His Arg Phe Ser Lys Arg Arg Asp Ser
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<210> 928

<211> 22

<212> PRT

<213> Homo sapiens

<400> 928

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Thr His Ala Ser Glu Pro
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<210> 929

<211> 3245

<212> DNA

<213> Homo sapiens

<400> 929

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344

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<210> 930

<211> 1479

<212> DNA

<213> Homo sapiens

<400> 930

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345

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<210> 931

<211> 1476

<212> DNA

<213> Homo sapiens

<400> 931

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 Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn Asn Phe Tyr
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International Bureau(43) International Publication Date
4 October 2001 (04.10.2001)

PCT

(10) International Publication Number
WO 01/073032 A3(51) International Patent Classification⁷: **C12N 15/12**,
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35/14, C12Q 1/6809/679,426 2 October 2000 (02.10.2000) US
09/685,166 10 October 2000 (10.10.2000) US
09/709,729 9 November 2000 (09.11.2000) US

(21) International Application Number: PCT/US01/09919

(71) Applicant (for all designated States except US): **CORIXA CORPORATION** [US/US]; 1124 Columbia Street, Suite 200, Seattle, WA 98104 (US).

(22) International Filing Date: 27 March 2001 (27.03.2001)

(72) Inventors; and

(25) Filing Language: English

(75) Inventors/Applicants (for US only): **XU, Jiangchun**

(26) Publication Language: English

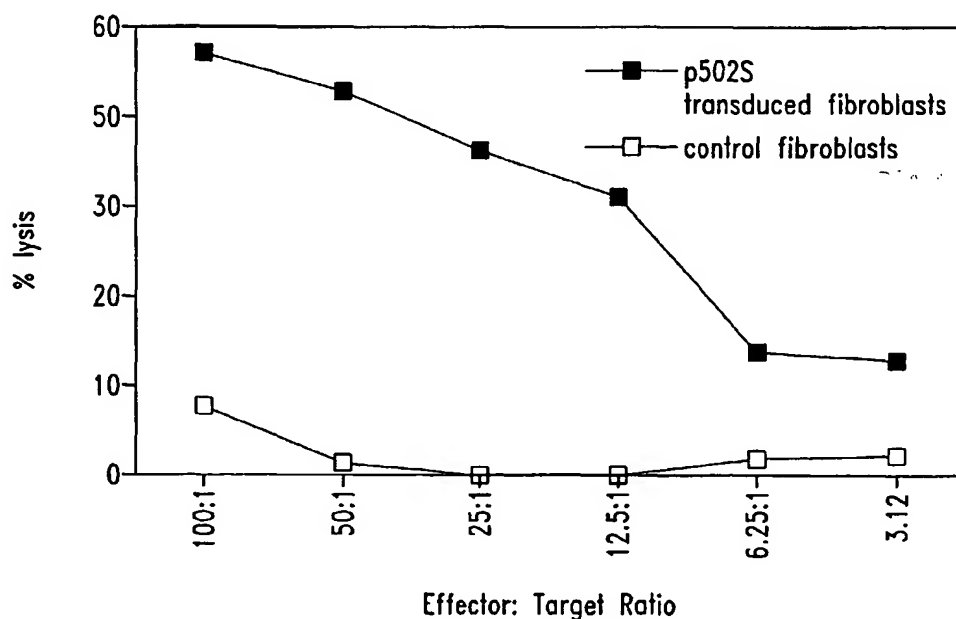
(30) Priority Data:

09/536,857	27 March 2000 (27.03.2000)	US
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09/593,793	13 June 2000 (13.06.2000)	US
09/605,783	27 June 2000 (27.06.2000)	US
09/636,215	10 August 2000 (10.08.2000)	US
09/651,236	29 August 2000 (29.08.2000)	US
09/657,279	6 September 2000 (06.09.2000)	US

[US/US]; 15805 S.E. 43rd Place, Bellevue, WA 98006 (US). DILLON, Davin, C. [US/US]; 18112 N.W. Montreux Drive, Issaquah, WA 98027 (US). MITCHAM, Jennifer, L. [US/US]; 16677 N.E. 88th Street, Redmond, WA 98052 (US). HARLOCKER, Susan, L. [US/US]; 7522 13th Avenue W., Seattle, WA 98117 (US). JIANG, Yuqiu [CN/US]; 5001 S. 232nd Street, Kent, WA 98032 (US). KALOS, Michael, D. [US/US]; 8116 Dayton Avenue N., Seattle, WA 98103 (US). FANGER, Gary, Richard [US/US]; 15906 29th Drive S.E., Mill Creek, WA 98012 (US). RETTER, Marc, W. [US/US]; 33402 N.E. 43rd Place, Carnation, WA 98104 (US). STOLK, John, A. [US/US]; 7436 N.E. 144th Place, Bothell, WA 98011

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.



WO 01/073032 A3



(US). **DAY, Craig, H.** [US/US]; 11501 Stone Avenue N., C122, Seattle, WA 98133 (US). **VEDVICK, Thomas, S.** [US/US]; 124 S. 300th Place, Federal Way, WA 98003 (US). **CARTER, Darrick** [US/US]; 321 Summit Avenue E., Seattle, WA 98102 (US). **LI, Samuel, X.** [US/US]; 3608 175th Court N.E., Redmond, WA 98052 (US). **WANG, Aijun** [CN/US]; 3106 213th Place S.E., Issaquah, WA 98029 (US). **SKEIKY, Yasir, A., W.** [LB/US]; 15106 S.E. 47th Place, Bellevue, WA 98006 (US). **HEPLER, William, T.** [US/US]; 12034 38th Avenue N.E., Seattle, WA 98125 (US). **HENDERSON, Robert, A.** [US/US]; 8904 192nd Street S.W., Edmonds, WA 98026 (US).

(74) Agents: **POTTER, Jane, E., R.**; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

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INTERNATIONAL SEARCH REPORT

Inte pplication No
PCT/US 01/09919

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C12N1/21 C12N5/10 C07K16/18
G01N33/68 C07K19/00 C12N15/10 A61K38/17 A61K31/70
A61K39/395 A61K35/14 C12Q1/68 C12N5/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 37039 A (TADA KEISHI ;SAKAI YUICHI (JP); ASAHI CHEMICAL IND (JP); KOBAYASHI) 27 August 1998 (1998-08-27)	1-9, 11-16
Y	the whole document SEQ ID NO 1	10,17
X	WO 98 37418 A (CORIXA CORP) 27 August 1998 (1998-08-27) the whole document SEQ ID NO 1	1-8, 11-16
X	WO 00 04149 A (CORIXA CORP) 27 January 2000 (2000-01-27)	1-17
Y	the whole document SEQ ID NO 1	10,17

	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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 "O" document referring to an oral disclosure, use, exhibition or other means
 "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
 "&" document member of the same patent family

Date of the actual completion of the international search

27 March 2002

Date of mailing of the international search report

15. 07. 2002

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INTERNATIONAL SEARCH REPORT

Inter ... lication No
PCT/US 01/09919

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 25272 A (CORIXA CORP ; REED STEVEN G (US); XU JIANGCHUN (US); CHEEVER MARTIN) 12 April 2001 (2001-04-12) claims 50-71 ---	9-17
E	WO 01 34802 A (HARLOCKER SUSAN L ; CORIXA CORP (US); DAY CRAIG H (US); JIANG YUQIU) 17 May 2001 (2001-05-17) claims 31-55 ---	9-17
E	WO 01 51633 A (FANGER GARY RICHARD ; HARLOCKER SUSAN L (US); MEAGHER MADELEINE JOY) 19 July 2001 (2001-07-19) claims -----	1-17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/09919

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 9 12 13 and 17 are (partially) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-17 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-17 partially

Polynucleotide with SEQ ID NO 1, the encoded polypeptide, antibodies against the polypeptide and their uses

Inventions 2-651: claims 1-17 partially

Polynucleotides with SEQ ID NO's selected from 2-942 as mentioned in claim 1, the encoded polypeptides, antibodies against the polypeptides and their uses

INTERNATIONAL SEARCH REPORT

 Into
 PCT/US 01/09919

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